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PRESIDENTIAL ADDRESS *

By ROGER I. LEE, M.D., F.A.C.P., *Boston, Massachusetts*

THIS Annual Session of the American College of Physicians, this Convocation is a significant demonstration of the determining philosophy upon which the College is founded. Others may speak of the education and training in the professions of religion, teaching, engineering, the law, business, etc., but in the profession of medicine, and particularly in the medical specialties of which our College is a noteworthy illustration, it seems desirable to discuss from time to time certain outstanding features. As a preface to this discussion one may recall the emphasis that the late Charles W. Eliot, then President of Harvard University, put upon what he called the "prodigious advances in Medicine." That phrase is as true today as it was 35 years ago, and if one reads the times correctly, it will be even more true in another 35 years. Some of the oldsters among us look back on our student and hospital days in which there were no gastrointestinal roentgen-rays, no blood pressure apparatus, no determinations of the basal metabolic rate. no electrocardiograph, no Wassermann test, no cunning dyes that helped our diagnostic pursuit, no intravenous therapy, and very little of what we now call Chemotherapy. I mention only a few of a staggering list. And what of those from our ranks who tried to practice medicine with the education and training that they received only from the Medical School even when supplemented by a hospital internship! In charity we draw a veil over the direful possibilities.

It is axiomatic that the four years immediately after graduation from Medical School are more important than the four years in the Medical School. And this is true despite the inestimable value of the fundamental education in the Medical School. Moreover, this is a continuing process throughout a man's active medical life. The oldsters in their daily routine, in active practice at the bedside, in the clinic, in the laboratory and in teaching use technics in diagnosis, treatment and in investigation that were unheard of in

* Address at the Annual Convocation of the American College of Physicians, St. Paul, Minnesota, April 22, 1942.

their student days. Side by side the oldsters and the youngsters learn together. The pace is "hot." The oldsters pant and sweat with the necessary exertion of learning the intricacies of the electrocardiograph or the electroencephalograph, for example, and of trying to understand the complexities and the inevitable jargon of immunology and of hormones, vitamins, and the like. But to stop is to be lost. It may be pride that drives us on, but I like to think that it is the excitement of the chase and the love of our profession. And I like to think that therein lies the enduring satisfaction of our professional lives. It is a satisfaction to recall that though inconspicuous and perhaps unsung and unquoted one took part in some of the prodigious advances in Medicine. As I have said before, that is and must be the fundamental philosophy upon which the American College of Physicians stands.

To those of you who are about to be received into Fellowship of the College, the College certifies that you have made notable progress in the Specialty of Internal Medicine. You know and the College knows that your progress has not always been easy. But mark you this, the College certifies only to your progress, not to your arrival at your professional destination. Only physical or professional death will mark the end of your progress. The excitement of these prodigious advances will, I fondly trust, continue to spur on your footsteps. These next years, I assure you, will be even more vital to your progress than the years that have gone before. The College hopes that this recognition of your progress in internal medicine will be accepted by you as evidence of your promise for the future. Your futures will be even more varied than your pasts. Some of you have already joined the armed forces of this country. Perhaps most of you will eventually join the Army or Navy. The rest of you will do double or makeshift duty in civilian practice, in the hospital, in teaching, or in the laboratory. This tremendous dislocation of your professional lives is your bit and is to be accepted as your job. For winning the war is at this moment the first and only job of every man, woman and child of this country, of every Fellow of this College and of the College itself.

There are, however, real possibilities of prodigious advances in Army and Navy medicine, even though there are restrictions imposed by military necessities. Some of you have already surmounted difficulties of a similar nature. Some of you undoubtedly have labored under the restrictions imposed by such circumstances as locality, finances, inadequate equipment, unfavorable surroundings. It is particularly to the credit of those when they have not only kept abreast of the rapid advances in medicine but also have kept their medical curiosity alert, so that on occasion they have pushed the frontiers forward.

If the slogan of successful modern warfare is the offensive, always the offensive, the slogan of successful modern medicine, and indeed of this College, might be the advance, always the advance, in the armed forces and in peace. We must keep our enemies of disease and ignorance always on the defensive by never being on the defensive but always attacking, by readily

shifting plans to meet new situations. Disease and germs, like the Japs and Germans, always seek the initiative and always wage totalitarian war.

I realize that I have given a bald outline of one aspect of the ideology of this College. The College has tried to substantiate this ideology. The College recognizes its obligations to its Fellows and its country in peace and war. The College does not content itself with its Annual Meeting and the publication of the ANNALS OF INTERNAL MEDICINE, important and indeed vital as these two undertakings are. All of us need help in keeping up the pace of medical progress, and this is even more true in war than in peace. I speak advisedly when I say that the College has not yet met this obligation adequately, but important beginnings have been made. In the winter and spring of 1941, under the auspices and supervision of the College, seven postgraduate courses in internal medicine and related subjects were conducted for members of the College and other qualified physicians in medical centers all over the country. During the winter and spring of 1942 a somewhat more extended postgraduate course program was planned. Eleven courses were scheduled at widely separated medical centers, but due to war conditions five of them had to be withdrawn. The Annual Session of the College is actually a postgraduate week with its diversified program of clinics, panels, morning lectures and general sessions. Throughout the year, numerous regional meetings of Fellows and Associates have been conducted. Your president can testify to the professional and scientific excellence of some of those regional meetings which he was able to attend.

The College is quite alive to the new problems and new difficulties of physicians who are Fellows, Associates or potential material for the College, who are in the armed forces of the country. Already the Advisory Committee on Postgraduate Courses of the College carried out a week's program of Postgraduate Nights consisting of 16 lectures for the benefit of Medical Officers at one of the large Naval Hospitals. Discussions have taken place with the appropriate authorities of the Army and Navy who are very cooperative, and it is hoped that this program may be developed and expanded. It is not too much to expect that, when and where the military situations allow, medical service in military hospitals may be comparable to service in civilian hospitals. This will mean, of course, the best of medical care to the soldiers and incidentally (and it must be incidental) the professional progress of the medical officers.

Many Fellows and Associates of the College are on active military duty. For them the College has reduced the annual dues and initiation fees. The war activities of the individual members of the College, who may not be fortunate enough to wear uniform, are manifold. All over the country, Fellows of the College, in addition to their ordinary duties, are serving as examining physicians, are on draft boards, advisory boards and on appeal boards. As the war tempo increases, there will be more demands for double duty and makeshift duties. Many pet researches of our Fellows must be laid aside for the duration.

The National Research Council drafted members of the College as individuals for service on its many committees. A former President of the College, Dr. O. H. Perry Pepper, is the hard working chairman of the Committee on Medicine of the National Research Council. I suspect that Dr. Pepper is more in Washington than in Philadelphia.

Well over a year ago, the College undertook to classify internists for possible availability for military service, according to capabilities, experience, age and other criteria. Your President-Elect, Dr. James E. Paullin, of Atlanta, has devoted himself without stint to this arduous task. By this forehanded action and with similar activities by the American Medical Association and the American College of Surgeons, information concerning the Medical Resources of the country was available when war was declared. Now President Roosevelt has appointed Dr. Paullin on all the important Committees of Procurement and Assignment. The Regents believe that the sum of $3500.00 appropriated for clerical and technical assistance for this work has more than amply been justified in its value to National Defense.

Over a year ago when no governmental funds were available, because the Regents of the College and the National Research Committee on Medicine believed the need was urgent, the College made an appropriation of $10,000.00 for the promotion of a research project of Dr. Edwin J. Cohn of the Harvard Medical School. This project concerned the preparation and adaptation of certain types of plasma for human transfusion. Dr. Cohn has told us of some of his work at one of the morning lectures of this Annual Session. The necessary restrictions imposed by the state of war has, of course, prevented Dr. Cohn from unfolding the whole fascinating story of his work. I like to think that these moneys are personal contributions of the Fellows of the College to National Defense, rather than the contribution of the College, which is impersonal.

Army medicine, naval medicine, aviation medicine, civilian medicine are in essence one and the same. Hence, in these Annual Sessions of the College, actually, as I have said before, a postgraduate week, there are papers in aviation medicine, on blood banks, on blood substitutes. There are papers on typhus fever, malaria, and tropical diseases. Such expert discussions have a direct relation to the war, the first group seemingly more than the second. But there will henceforth always be civilian aviation. Aviation is an important method of transportation today. There will be transfusion of blood and of blood substitutes in peace times. The medical problems discussed in all the clinics, panels, lectures and papers have application in both military and civil life. Yes, and I include geriatrics as a military problem. What makes a colonel or a general unfit at 60, or before 60, or not until 70? How can we select the men? And more important, how can we keep them fit? And, if this applies to the army, it applies peculiarly to the defense effort and it applies to civilians in times of peace. At this time the College has but a single purpose, that of winning the war, but the College believes that in war and in medicine, the secret of success is the offensive, the advance, the attack and always and ever so.

CLINICAL–PATHOLOGICAL CONFERENCE *

DISCUSSER—WALLACE M. YATER, M.D., F.A.C.P., *Washington, D. C.*
PATHOLOGIST—CHARLES F. BRANCH, M.D., *Boston, Massachusetts*

DR. YATER: After having read the history of the case we are to discuss this morning, I am convinced that there are just as hard medical nuts to crack in Boston as there are in Washington and elsewhere. I approach a discussion of this case with fear and trepidation, and hope it will not turn out to be a Dunkirk for me.

May I suggest that we refresh our minds concerning this rather mystifying case by reading it over again together from beginning to end.

CLINICAL HISTORY

The patient was a 35 year old man, by occupation a wood-worker. When he was 18 years old he had an attack of appendicitis with appendectomy under chloroform and ether anesthesia. He had a prolonged convalescence from this operation with drainage of an appendiceal abscess. On several occasions when the dressings were being changed and drains were inserted, chloroform anesthesia was necessary. However, the recovery from this illness was said to be complete.

Six years ago, when he was 29 years old, he had an attack of lobar pneumonia followed by a sterile pleural effusion which subsided after aspiration. At about this time he commenced to have recurrent attacks of mild transitory jaundice.

About a year ago he began having attacks of fever, usually accompanied by diarrhea. There would be a sudden chill, high fever, and the passage of several loose stools. The fever would last from 24 to 36 hours and then subside. Between attacks of chills and fever and diarrhea he felt quite well. At first the chills and fever occurred nearly every week. He entered one of the Boston hospitals for study, remaining there for eight weeks. Under observation he was found to have an irregular, low-grade fever which ranged between 98.6° F. and 100° F., occasionally interrupted by chills when his temperature would be 102° F. or 103° F.

On physical examination the skin was normal in appearance. The heart and lungs were negative except for a systolic murmur at the apex; no diastolic murmur was heard. The spleen was palpable two fingers' breadth below the costal margin. The rest of the physical examination was negative. Numerous blood cultures were negative. Agglutination tests for undulant fever and for typhoid and paratyphoid fevers were negative. Gastrointestinal roentgen-ray series, films of the chest, intravenous pyelograms, and barium enema all were negative. The electrocardiographic tracing showed slurring of the QRS complexes, suggestive of an intraventricular conduction defect. On one occasion it was said that the patient had a shower of petechial hemorrhages over the skin, and in one blood smear a monocyte was found with an engulfed red cell. In view of the extensive oral sepsis which the patient presented, numerous teeth were removed, but this procedure appeared to have no effect on either the chills or fever.

The patient finally was discharged from the hospital, returning for follow-up study on two different occasions, one in two months and one six months later. He

* One of the Clinical-Pathological Conferences given at the Annual Meeting of the College in Boston on April 22, 1941, under the direction of Dr. Reginald Fitz.

stated that he had been reasonably well after leaving the hospital except for one or two bouts of fever with the temperature going to 103° F.

About six months after his last return to the hospital he entered the Robert Dawson Evans Memorial Hospital for further study. At this time he complained of recurrent attacks of chills and fever, and of a distended abdomen. The distention was of recent onset and caused no great discomfort.

The skin was pale and there were numerous telangiectatic spots over the arms and shoulders. Such spots typically had raised central areas which were red and from whose central point numerous small blood vessels radiated outward. When gentle pressure was exerted over these telangiectatic areas, pulsation of their smaller arterioles could be seen. The eyegrounds were normal.

The lungs were clear throughout. The heart was not enlarged; there was a soft systolic murmur at the apex, but no diastolic murmur was heard. The blood pressure was 110 mm. Hg systolic and 70 mm. diastolic. The abdomen was slightly distended. The spleen was palpable in the left upper quadrant, extending 3 cm. below the costal margin on deep inspiration. The liver was not felt. No other masses were palpable. There was a right-sided hydrocele and slight pitting edema over the ankles and sacrum.

The blood Wassermann reaction was negative; the hemoglobin was 70 per cent, with a red blood cell count of 3,500,000; the white cell count was 4,000; differential count of the leukocytes was normal. The nonprotein nitrogen ranged between 31 to 44 mg. per cent; the blood cholesterol ranged between 250 to 300 mg. per cent; the serum bilirubin ranged between 1.3 and 4.3 mg. per cent. The sedimentation rate was elevated above normal. The Takata-Ara test was positive in all dilutions; the total protein of the blood was 5.7 gm. per cent; of this the albumin was 2.5 gm. and the globulin 3.2 gm. per cent. Agglutination tests for the typhoid-paratyphoid group were negative. The bromsulfalein test showed 40 per cent retention of the dye at the end of half an hour with 50 per cent retention at the end of five minutes. Repeated examinations of the urine showed no albumin or sugar; bilirubin was present on six occasions, and urobilinogen always was increased in dilutions of 1 : 50 to 1 : 600; cultures of the urine were negative. Renal function appeared normal as judged by the phenolsulphonephthalein test, there being an excretion of 67 per cent in two hours. Electrocardiographic tracings continued to show a constant slight intraventricular conduction defect. Roentgen-ray films of the heart and lungs were negative. The barium enema was negative.

The patient remained under observation in the hospital for 67 days, and during this time he had several sudden bouts of fever which lasted between 24 and 36 hours. On two different occasions during the period of fever, blood cultures were positive for colon bacilli. During the period of hospital observation the patient's abdomen became notably distended and there developed definite signs of ascites. The ascitic fluid removed had a specific gravity of 1.004; its protein concentration was 0.68 gm. per cent, and of this the albumin concentration was 0.33 gm. and the globulin concentration 0.35 gm. per cent; the ascitic fluid sediment was negative. As a terminal event the patient developed tenderness in the left side of the neck with brawny induration and edema. This was associated with high fever, leukocytosis and delirium. At this time hemolytic streptococci were obtained from the throat on culture. The induration and edema in the neck continued to spread.

Clinical Discussion

There are certain disadvantages confronting the discusser of a case with which he has had no personal connection. He has to accept the results of observations of others without having an opportunity either to check them

or to extend them. On the other hand, he has the definite advantage of seeing the case as a whole and not piecemeal as does the attending physician. This is the same advantage that a consultant often has over the general practitioner who has seen the development of a case in its early phases, who may have been confused by the early indefinite symptoms, and who perhaps may not have examined the patient sufficiently often as the illness developed.

Now in this case, I shall take advantage of my privilege by beginning my discussion of the case near the end of its course. The data in the second from the last paragraph of the clinical history indicate definitely that the patient finally developed advanced disease of the liver, as indicated particularly by the retention of bromsulfalein, the positive Takata-Ara test, and the increase in the amount of urobilinogen in the urine. The bromsulfalein test, when positive, is quite specific as an indicator of advanced liver disease when there is little or no jaundice. The Takata-Ara test, though not specific, is quite suggestive of cirrhosis of the liver, when positive. A definite increase in the urobilinogen output is quite definitely an indication of hepatic disease. Other findings which support the diagnosis of serious disease of the liver, and particularly cirrhosis, are the anemia, the leukopenia, the moderately elevated blood cholesterol, the reversal of the albumin-globulin ratio, the fluctuating level of the serum bilirubin with moderate increase, and the later development of definite signs of ascites. The spleen was also palpable, and moderate splenomegaly is common with cirrhosis of the liver. The liver could not be felt and may, therefore, well have been shrunken. The presence of a hydrocele and slight pitting edema of the ankles and sacrum are consistent with the diagnosis of cirrhosis of the liver, and are no doubt due largely to the depression of the serum albumin level. On his last admission it was noted that there were numerous telangiectatic spots over the arms and shoulders. A description of these lesions indicates that they were the so-called spider nevi, which, when present, are practically pathognomonic of cirrhosis of the liver. Examination of the ascitic fluid indicated that it was a transudate and not an exudate.

The last paragraph of the clinical history shows that the final episode in this patient's life was his development of an intercurrent infection, consisting of two phases: colon bacillus bacteremia, and finally a cellulitis of the neck. It is, of course, not unusual for patients with cirrhosis of the liver to develop an infection terminally, which their lowered resistance does not allow them to overcome.

Having established the point that the patient's illness terminated with cirrhosis of the liver and the terminal intercurrent infection, let us return now to the history of the case, to see whether we may determine the cause and type of this cirrhosis. The patient was a wood-worker, but the history does not state what type of wood-worker. So far as I know, there is nothing in the occupation of wood-workers that could remotely lead to cirrhosis of the liver. However, the history states that chloroform anesthesia was

used several times for surgical purposes when the patient was 18 years of age. Recovery, however, was complete, and although chloroform sometimes produces serious liver damage, it is the type of liver damage from which recovery is complete unless the patient succumbs to it soon after the administration of the chloroform. Furthermore, the patient's chronic illness which led to his death did not apparently begin until 11 years later, when he was 29 years old. Therefore, I believe we can safely rule out the use of chloroform in the etiology of the disease of the liver.

Six years before the patient died, when he was 29 years old, he had an attack of lobar pneumonia, soon after which he began to have recurrent attacks of mild transitory jaundice. The etiology of the pneumonia is not stated in the history. However, streptococcal pneumonia and pneumococcal pneumonia are both occasionally complicated by cholangitis; and since the pneumonia was the only definite infectious disease from which the patient suffered, which might have played a rôle in the etiology of the disease of the liver, the possibility that it was important in this connection cannot be overlooked. Therefore, I believe we should assume that the patient may have developed a low-grade chronic cholangitis as a result of his pneumonia.

Certainly the subsequent course of the patient's illness following the pneumonia, particularly during his last year of life, was very suggestive of chronic cholangitis. He had exacerbations of the chronic infection, associated with sudden chills, high fever, and diarrhea. Diarrhea sometimes occurs in connection with cholangitis. Between these brief exacerbations the patient was quite well, but while under observation for eight weeks in one of the Boston hospitals it was noted that he had an irregular low-grade fever even between the more severe episodes.

The fourth paragraph in the history is designed to confuse us, not consciously on the part of the historian, but because of the facts contained therein. A systolic murmur at the apex was noted, but apparently without cardiac enlargement. The murmur itself need not be important. The spleen was noted to be palpable. This finding may be present with many infectious diseases, one of which is bacterial endocarditis. However, numerous blood cultures were negative, and there were no other features to suggest that diagnosis. Agglutination tests for certain of the prolonged fevers were negative. Diseases of the gastrointestinal tract, lungs, and urinary tract were ruled out by roentgen-ray and other studies. The electrocardiograms, to which we do not have access, showed slurring of the QRS complexes, but this finding in itself is of no importance in the consideration of our case, since it may occur under many circumstances. The one shower of petechial hemorrhages over the skin should not confuse us, since it was a transient episode, and one that might occur in many conditions. The removal of numerous teeth without effect upon the chills or fever was merely another instance of the fallacy of our theory of focal infection, which is beginning to "go by the board."

The course of the illness continued much the same way throughout, with longer or shorter remissions, until the terminal phase marked by the presence of advanced disease of the liver.

We have now come to the point where it is necessary to tie up our diagnosis of cirrhosis of the liver with the history of long-standing infection and bouts of chills, fever, and diarrhea. Laennec's cirrhosis does not follow such a clinical course, but there is a form of biliary cirrhosis, quite rare, which has been called cholangitic induration of the liver, or cholangitic cirrhosis. It is not the result of obstruction of the extrahepatic bile ducts but of chronic recurrent intrahepatic cholangitis. In this condition the liver becomes smaller and firmer and its surface more or less granular. When the liver becomes greatly shrunken by the periportal fibrosis, a secondary result of the shrinkage is portal congestion, and then splenomegaly and even ascites may appear. I believe that this case fits well the description of this rare disease.

In conclusion, I believe we can predict, if our ratiocination is correct, that the pathologist will show us a small, hard, granular liver, which microscopically shows an extreme degree of fibrosis primarily involving the intrahepatic biliary tract, but secondarily causing obstruction also to the portal radicles. There should be very little functioning liver parenchyma left.

Pathological Discussion

Dr. Branch

The pathologist accustomed to viewing the cumulative result of years of disease not infrequently finds it difficult to assess with mathematical accuracy all of the facts before him. Even with the aid of a complete clinical history and the facts marshaled by long microscopical study, one frequently finds that all is still not clearly explained. To one with such experiences behind him, Dr. Yater's brilliant and clairvoyant discussion is most refreshing, and I am given to wonder if the good internist was not looking over my shoulder at the necropsy. His analysis is so perfectly accurate down to the last detail that it must perforce bespeak his great clinical ability.

As has been so carefully differentiated, the patient had no intrinsic heart disease, clinical signs and symptoms to the contrary notwithstanding. The heart weighed but 210 grams and showed no gross pathological changes. There was no histological evidence of rheumatic fever or other pathologic findings of consequence.

The lungs were also essentially negative, presenting only a slight terminal hypostatic pneumonia. A partially obliterative fibrous pleuritis on the right attested the pleural effusion which was a sequel to his pneumonia six years ago.

The gastrointestinal and genitourinary systems were essentially negative.

As pointed out, patients with cirrhosis frequently become so debilitated that their resistance is lowered and terminal bacterial invasion is frequent. In this instance the terminal *Bacillus coli* bacteremia and the cellulitis of the

neck were such manifestations. The importance of the bacteremia is difficult to estimate for it had given rise to no demonstrable focal lesions. The cellulitis of the left side of the neck with formation of an abscess about the left lobe of the thyroid yielded *Streptococcus hemolyticus* but no *Bacillus coli*. The carotid sheath was involved in this process, and there was also a small streptococcus-containing abscess just behind the sternal notch.

The splenomegaly of 400 grams, which could be palpated 3 centimeters below the costal margin, was primarily the response to a simple passive congestion due to the advanced liver obstruction. However, it also showed a well defined acute splenitis commensurate with the degree of cellulitis in the neck.

The extrahepatic biliary system and the pancreas were entirely negative. The gall-bladder contained no stones; all ducts were patent and showed no evidence of thickening or occlusion.

With all the clinical evidence at our disposal, one can hardly escape the outstanding picture of profound chronic liver disease. We have been much impressed with the development of this angle of the case by the discusser and heartily concur in the many aspects of his clear differential diagnosis. The chloroform episode was obviously a "red herring." The development of intermittent jaundice following the patient's pneumonia is much more suggestive of the true nature of his liver pathology. As has been so neatly drawn to your attention, during the past year at least, the patient has suffered from a marked chronic cholangitis.

With this outline so sharply stenciled on your canvas, little remains for me to do but fill in the colors. The liver presented a truly remarkable picture. It weighed but 775 grams, yet presented none of the external characteristics of the healed stage of acute yellow atrophy or toxic cirrhosis. It was extremely firm, relatively regular in outline and in general was pale yellowish-brown. Its entire surface was diffusely and uniformly studded with myriad minute, bright orange-brown nodular elevations, averaging 2 to 3 millimeters in diameter. The intervening capsule showed a dense fibrous thickening, and no normal lobulations could be discerned. Because of its density the organ was sectioned with difficulty. Multiple serial sections reveal the entire liver uniformly replaced with myriads of minute, golden-brown, plateau-like elevations 3 millimeters in diameter, roughly corresponding to the normal lobulations. The intervening stroma was depressed and consisted of glistening gray fibrous tissue. The interlobular bile ducts were thickened and projected slightly from the surrounding fibrous tissue. They were rather sharply defined by their contents, which consisted of granular, cloudy, pale greenish-brown, mucoid bile. There was no gross evidence of bile stasis in the smaller canaliculi.

Histologically, the picture was entirely typical of the entity described by Dr. Yater. The outline of the original lobules was well preserved, and, if anything, accentuated by a marked increase of connective tissue in the periportal canals. The remaining parenchyma was arranged in a normal

fashion about the central veins, and in general consisted of liver cords which were hyperplastic. At some points they showed various stages of degeneration, whereas in other regions they were definitely regenerating. Near the periphery of some lobules were minute areas of focal necrosis, in which two or more liver cells were being invaded by neutrophiles. At the periphery the lobules were gradually destroyed by the recurrent acute attacks, so that now the portal canals are replaced by bands of connective tissue, actually 1 to 2 millimeters in width. These old battlefields contained all sorts of mementos of previous engagements. The scarring was profound. Large numbers of lymphocytes, plasma cells and monocytes infiltrated this entire zone, and the progressive nature of the lesion was further indicated by large periductular accumulations of neutrophiles and a rare eosinophile. The larger ducts were relatively constricted by the surrounding infiltration and scar tissue, and their lumina contained the partially inspissated, semipurulent bile noted above. The smaller bile ducts gave an erroneous impression of being increased in number; their epithelium was intact and they were virtually occluded by the surrounding induration. The intralobular canaliculi showed more evidence of bile stasis than was suggested by the gross picture, but in nowise comparable to the degree of dilatation observed in a true obstructive biliary cirrhosis. There was no central necrosis nor any pathologic change compatible with the suggested injury created by chloroform poisoning.

Thus, we have a liver showing a true cholangitic induration, or if you wish, an infectious biliary cirrhosis; a liver which in the early stages of the disease was larger than normal and at that time would have shown an acute infectious hepatitis; one which now is a rock-like monument to successive waves of exacerbation and remission, each receding line clearly marked in its remaining and totally insufficient architecture.

In closing we must admit that the microscope did no more for us, nor brought us no less certainly to the correct conclusion than did the illuminating remarks of the discusser.

PRIMARY CARCINOMA OF THE LUNG (REPORT OF 115 CASES, 38 AUTOPSIES AND 77 BRONCHOSCOPIC BIOPSIES) *

By J. A. PERRONE, M.D., and J. P. LEVINSON, M.D.,
Pittsburgh, Pennsylvania

ROSAHN [1] states that definite criteria for diagnosis should be established to render valid any comparisons of the incidence of carcinoma of the lung at different periods. These criteria are:

1. An autopsy must have been performed.
2. The carcinomatous nature of the lesion must have been verified microscopically.
3. There must be no reasonable doubt that the neoplasm was a primary growth.
4. Percentage should be calculated on the basis of total adult necropsies. Rosahn arbitrarily adopts 20 years as the lower age limit.

In our report we have attempted to fulfill all of the above criteria. We have an autopsy series of 38 primary carcinomas of the lung occurring in the years 1911–1939 inclusive, and 77 cases of bronchoscopic biopsies during 1933–1940, in which a pathological diagnosis of carcinoma was made.

INCIDENCE

Simons [2] in his monograph has reached the following conclusions regarding incidence.

1. Incidence of the disease has increased absolutely and relatively.
2. Continued suggestions that such an increase is only apparent and not real are denied by the facts.
3. The increases were gradual until the early 1900's, since when the gradient of increase has become constantly steeper.
4. In many localities the greatest incidence seems to have been reached in 1924, whereas in others the frequency still is advancing.

In general it can be stated that 1 to 2 per cent of necropsies reveal lung cancers and that 10 per cent of all cancers at autopsy are lung cancers.

All these factors concerning incidence are, in general, borne out in our group of cases. For example in table 1 we see the great increase in lung cancers whereas carcinomas of the stomach and colon were remaining relatively constant.

* Received for publication August 17, 1940.
From the Departments of Bronchoscopy and Pathology, Mercy Hospital, Pittsburgh, Pa.

TABLE I

Year	Ca. of Stomach	Ca. of Colon	Ca. of Lung	Total Autopsies
1911–21.....	21 or 3.4%	7 or 1.1%	5 or .81%	614
1922–32.....	14 or 3.5%	14 or 1.2%	17 or 1.5%	1,158

From 1911–1939 there have been 2,694 necropsies at the Mercy Hospital; of these there has been a total of 359 carcinomas. This would then make lung carcinoma 13 per cent of all carcinomas. This figure coincides rather closely with that generally given.

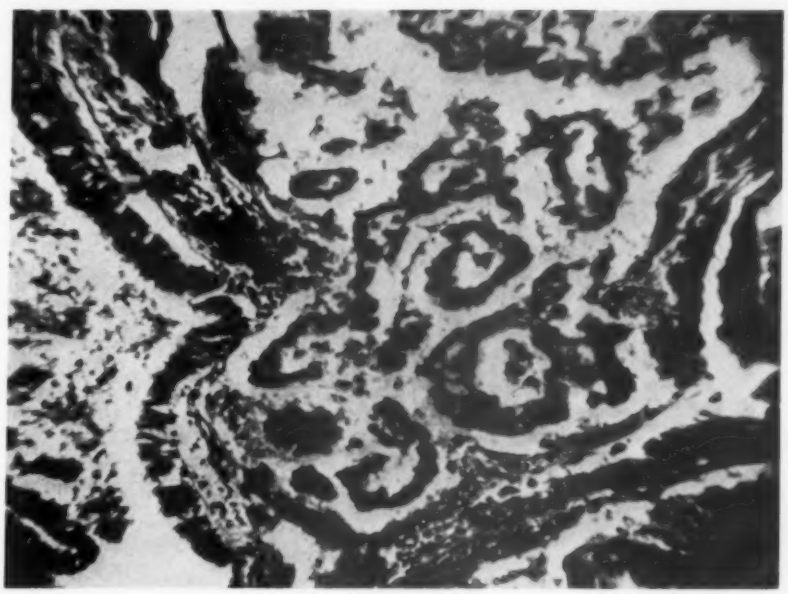

FIG. 1. Adenocarcinoma type (× 125). Glandular structures shown beneath the epithelium lining a bronchus. *Note:* This patient was a fireman. He dated the onset of his symptoms from a fire during which he inhaled a great deal of smoke. This was a year before admission.

ETIOLOGY

The etiological factor here as in other carcinomas is still a mystery. The various factors suggested are heredity, trauma, pulmonary tuberculosis, influenza, pneumoconiosis, chronic pulmonary diseases, roentgen-ray, dust inhalation, tin particles, motor exhaust fumes, war gases, occupational hazards, tobacco smoking. Simons [2] concluded that no single etiologic agent could be pointed out as the cause of pulmonary cancer. He states, "In any event, all known etiologic agents have in common the one characteristic of producing pulmonary irritation and, since they are so diverse, the only conclusion possible is that such irritation is the real activating or causative factor in the disease. This is not to say, of course, that all chronic pulmonary irritations

ensue in carcinomas; and it is to be hoped that future research will make this definition of the cause either more specific or more conclusive or both."

TABLE II

Autopsy Series

Previous Respiratory Infection	Number	Percentage
Asthma	1	2.6
Bronchiectasis	1	2.6
Bronchitis	3	7.8
Influenza	3	7.8
Pneumonia	4	10.5
Tuberculosis	1	2.6
No previous respiratory infection	25	65.7
Total	38	

Note: Two cases had lung abscess. One case had active tuberculosis.

Bronchoscopic Series

Previous Respiratory Infection	Number	Percentage
Bronchitis	3	3.7
Diphtheria	1	1.4
Influenza	8	10.5
Pleurisy	1	1.4
Pneumonia	20	25.8
No previous respiratory infection	44	57.2
Total	77	

TABLE III

Autopsy Series			Bronchoscopic Series		
Tobacco Smokers	Number	Percentage	Tobacco Smokers	Number	Percentage
Heavy	2	5.2	Heavy	16	20.7
Moderate	4	10.5	Moderate	22	28.5
Not smokers	32	84.2	Not smokers	39	50.6
Total	38		Total	77	

Wells and Cannon [3] report a case in which localized trauma appeared to be the exciting factor in the production of a lung cancer.

In our study we have been unable to find any specific etiologic factor. Some investigators have considered influenza as an etiologic factor but we would raise the question whether or not the manifestations of influenza may not often be an early sign of the pulmonary tumor. The occupations of our patients are listed in table 4.

Sex Incidence. In general, as reported by Overholt,[4] there are three males to every female. This has remained fairly constant in spite of the increased tendency of women to smoke. In our autopsy series we have had 34 males and 4 females, and in the bronchoscopic series we have had 61 males and 16 females.

TABLE IV

Autopsy Series Occupation	Number	Bronchoscopic Series Occupation	Number
Business man	1	Barber	2
Carpenter	4	Brass worker	1
Chipper steel mill	1	Butcher	1
Coal miner	2	Clerk	5
Electrical craneman	1	Clothes presser	1
Envelope cutter	1	Construction worker	1
File clerk	1	Cook	1
Fireman	1	Electrician	1
Garage man	1	Engineer	1
Housewife	1	Florist	1
Janitor	1	Glass worker	1
Laborer, steel mill	1	Housewife	15
Mill foreman	1	Laborer	8
Minister	1	Machinist	4
Open hearth worker	1	Merchant	2
Oyster opener	1	Metal worker	2
Painter	1	Mill worker	1
Scrapman	1	Miner	8
Store keeper	1	Painter	2
Transfer bus	1	Physical education instructor	1
Transportation Co. official	1	Postmaster	1
Traveling salesman	1	Printer	1
Truck driver	1	Produce peddler	1
Unknown	11	Retired	12
		Salesman	2
		Tanner	1
Total	38	Total	77

TABLE V

Autopsy Series			Bronchoscopic Series		
Sex	Number	Percentage	Sex	Number	Percentage
Male	34	89.5	Male	61	79.3
Female	4	10.5	Female	16	20.7
Total	38		Total	77	

Age Incidence. There have been about 13 cases reported in the literature occurring below the age of 19. The youngest we have been able to find is a questionable case occurring in a child of seven. Our youngest patient was 23 and the oldest 76.

TABLE VI

Autopsy Series			Bronchoscopic Series		
Age	Number	Percentage	Age	Number	Percentage
20–30	0	0.0	20–30	2	2.3
30–40	4	10.5	30–40	5	6.5
40–50	10	25.5	40–50	10	12.9
50–60	15	39.5	50–60	30	38.9
60–70	6	15.5	60–70	24	31.4
70–80	3	9.0	70–80	6	7.7
Total	38		Total	77	

Color Incidence. An interesting feature has been the absence of negroes in the autopsy series, and the occurrence of the lesion in only two negroes in the bronchoscopic series. This is probably owing to the relatively small

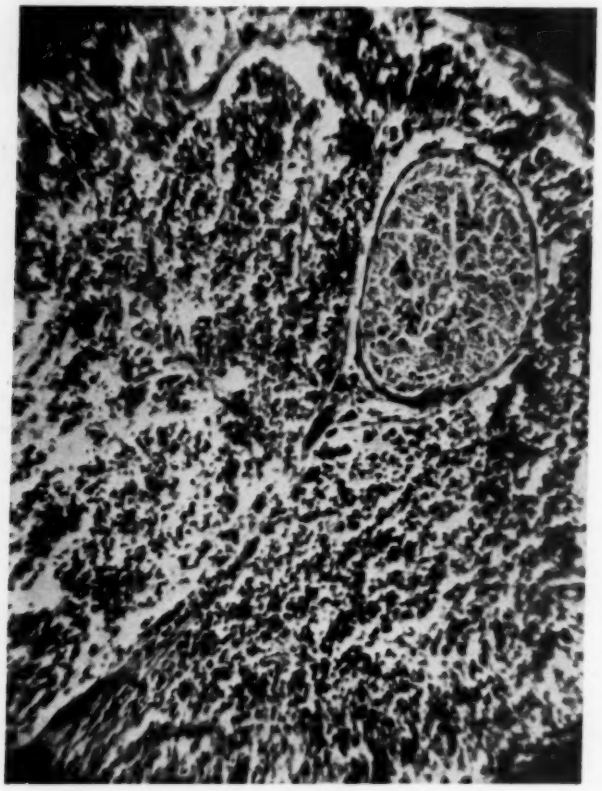

FIG. 2. Small round cell type (× 125).

negro population at our hospital. D'Aunoy,[5] in a series of 74 autopsies from the Charity Hospital in New Orleans, reported 47 white patients and 27 negroes. There is of course a much larger negro population at that institution. In general we believe that lung carcinoma is relatively rarer in the colored race.

TABLE VII

Autopsy Series		Bronchoscopic Series		
Race	Number	Race	Number	Percentage
White	38	White	75	97.4
Negro	0	Negro	2	2.3
Total	38	Total	77	

Pathology

There have been numerous classifications of lung carcinoma based on the macroscopic appearance. Grossly, the tumor occurs most commonly as an infiltrating type of lesion usually beginning at the hilus and extending through the lung parenchyma. There are two other general types, one a diffuse growth resembling a pneumonia or miliary tuberculosis, the other, the multiple nodular type in which the primary tumor may be minimal with wide-spread metastases both in lungs and elsewhere.

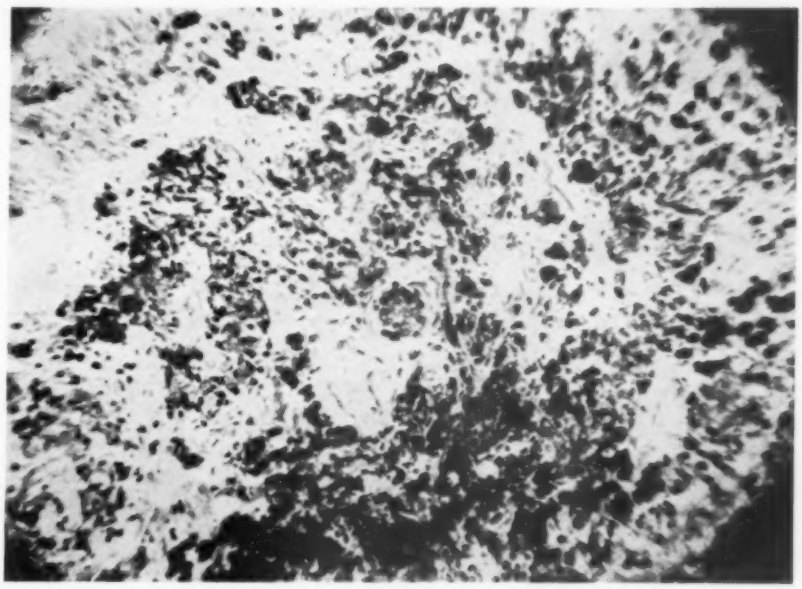

Fig. 3. Large polyhedral cell type (× 125).

The masses of tumor tissue are usually gray, white or pink on cross section. Often one finds many necrotic areas filled with material resembling pus or mucus. This is often mistaken for tuberculosis or even pneumonia.

To quote from Simons [2]: "In the earliest stages, according to Tuttle and Womack, one sees a piling-up of the mucous membrane with a gradual extension along the mucosa and out into the bronchial lumen. The picture becomes one of a fanshaped grayish mass extending out into the lung parenchyma with various stages of necrosis and abscess formation. Less often one sees the tumor as a diffuse growth involving an entire lobe or even a whole lung, thus giving a picture not unlike that seen in the gray hepatization of pneumonia. Rarely the tumor may be found as single or multiple nodules in the parenchyma of the lung with no apparent connection with the larger bronchi."

The most common associated lung changes in Arkin and Wagner's [8] series of 74 cases (Simons), were pleural effusion (47 per cent), bronchiec-

tasis (43 per cent), acute pneumonia (28 per cent), chronic pneumonia (20 per cent), abscess or gangrene (20 per cent) and purulent bronchitis (19 per cent). The manifestations of pulmonary carcinoma clinically and pathologically are so diverse that the diagnosis is difficult. As Hruby and Sweany [9] have stated, tuberculosis is the most common disease confused with primary carcinoma of the lung.

In general, the bronchial origin is demonstrable according to most investigators in about 70 per cent of cases. Sweany [6] has stated, "If there

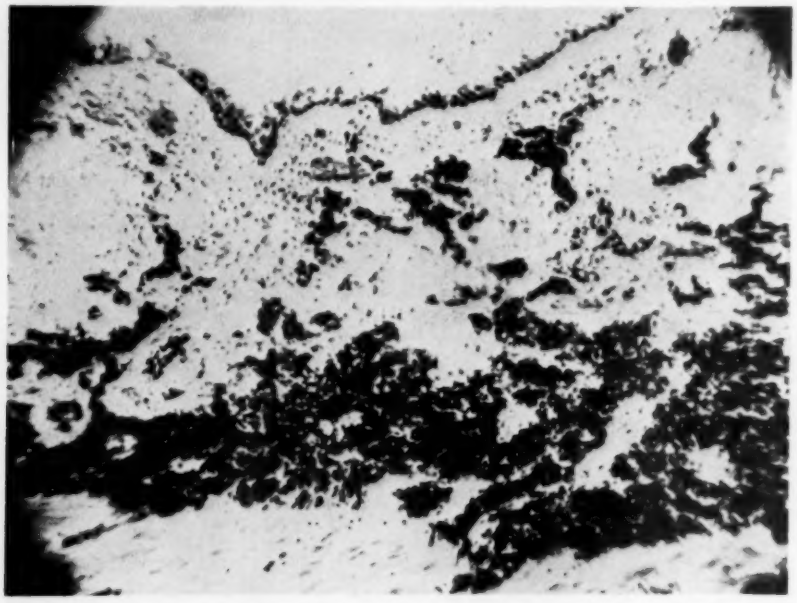

FIG. 4. Oat cell type (× 125). Nests of tumor cells are shown in a loose stroma beneath a layer of bronchial epithelium.

is any merit to the theory of origin from bronchial mucosa it will necessitate the proof of some form of metaplasia from one type of tissue to another." An injury to bronchial lining usually heals. If a malignant tendency exists, carcinoma may result and there seems to be a multiple potential nature in the basal cells. Cancers arising from the pulmonary alveoli are very rare, if they exist at all. There is still some question as to whether the lining of the alveoli is epithelial or mesothelial. We feel, as most investigators do, that the latter is true. Womack [7] has stated that carcinomas which arise in the periphery of the lung are more rapidly fatal than those arising at the hilus. He explains this on the basis of more rapid spread by way of lymphatics to the hilar nodes.

The present accepted theory of origin of the various cell types of lung carcinoma is that of Fried [10] (Simons). He summarizes his belief by stating that of the cells lining the bronchial mucosa, that is, the ciliated columnar,

the goblet, and the "basal" cells, only the last are concerned in the process of regeneration of the bronchial mucous membrane. It is evident, therefore, that these cells likewise serve as a sole matrix for primary bronchiogenic tumors. And third, primary squamous cell epitheliomas and basal cell epitheliomas of the lungs do not result from metaplasia of preëxisting ciliated columnar epithelium, but originate through protoplasia or indirect metaplasia of the undifferentiated basal cell of the bronchial mucous membrane. D'Aunoy [5] chooses to call the undifferentiated basal cell the "reserve cell." We have divided our cases into adenoid, squamous, and undifferentiated types. In the latter we have described basal cell, round cell and large polyhedral cell types.

TABLE VIII

Autopsy Series

Cell Type	Number	Percentage
Adenoid	7	18.4
Squamous	9	23.6
Undifferentiated:		
Large polyhedral	4	10.5
Oat cell	12	31.5
Round cell	6	15.7
Total	38	

Note: In many of the tumors there was a mixture of various cell types. The above classification is made on the predominant type of cell. Two of our autopsy cases were originally diagnosed in 1916–17 as lymphosarcoma. A review of the slides shows that these were actually primary carcinomas of lung. This was formerly a rather common error in diagnosis.

Bronchoscopic Series

Cell Type	Number	Percentage
Adenoid	3	4.0
Squamous	28	36.3
Undifferentiated:		
Large polyhedral	13	16.8
Oat cell	24	31.2
Round cell	9	11.7
Total	77	

METASTASES

The usual order of frequency is: (1) regional lymph nodes, (2) liver, (3) lungs, (4) bones, (5) kidneys, (6) adrenals, (7) pleura, (8) brain, (9) pericardium, (10) pancreas, (11) cervical lymph nodes, (12) heart, (13) thyroid, (14) spleen. Metastases occur by blood and lymph stream. One factor supporting blood stream metastasis is that breast and pulmonary carcinomas furnish the highest percentage of secondary new growths in the cranial cavity.

It has been stated in general that the right lung, especially the upper lobe, is most frequently involved. This is also apparently true in pulmonary tuberculosis. The reason for this is not evident. The fact that this portion of the lung is most subject to irritative factors may have some significance.

TABLE IX

Autopsy Series

Metastases	Number
Regional lymph nodes:	
Peribronchial	22
Mediastinal	13
Supraclavicular	4
Retroperitoneal	4
Mesenteric	4
Liver	13
Pleura	12
Pericardium	10
Opposite lung	8
Subcutaneous tissue	6
Kidney	6
Heart	5
Pancreas	5
Adrenal	4
Diaphragm	4
Aorta	3
Esophagus	3
Spleen	3
Trachea	2
Gall-bladder	2
Bone	2
Thyroid	1
Brain	1

Note: There was one case in which the spinal fluid suggested brain metastasis, but permission was not granted for prosection of the head. In another case permission was granted only for examination of the lung.

TABLE X

Autopsy Series

Frequency of Side Involved	Number	Percentage
Right lung	25	65.7
Left lung	13	34.2
Total	38	

Note: There was also a tendency in our series to find the upper lobes involved more frequently than the lower. Thirty-six of our cases showed the infiltrating type of lesion. One was a diffuse adenocarcinoma resembling gray hepatization and one was a multiple nodular type.

Bronchoscopic Series

Frequency of Lobes Involved	Number	Percentage
Right main bronchus	6	7.7
Left main bronchus	7	9.7
Right upper lobe	13	16.6
Left upper lobe	4	5.2
Right lower lobe	34	44.1
Left lower lobe	9	11.6
Both lower lobes	1	1.4
Right middle lobe	2	2.3
Right middle and lower lobes	1	1.4
Total	77	

BRONCHOSCOPIC FINDINGS

Bronchoscopy is the one certain method by which carcinomas of the lung can be diagnosed early. Nearly 80 per cent of the primary lung carcinomas are situated in one of the main bronchi in which visualization is within range.

In these, a biopsy can be taken with ease. In many of the remaining cases, if no growth is seen within the bronchus, one can make an almost certain diagnosis if there is fixation of the involved bronchus.

Bronchoscopy is a safe procedure when performed by a trained endoscopist. No patient who presents a dry cough, wheezing or shortness of breath should be denied a bronchoscopic examination regardless of whether he is in the cancer age or not. Often with minimal physical signs and neg-

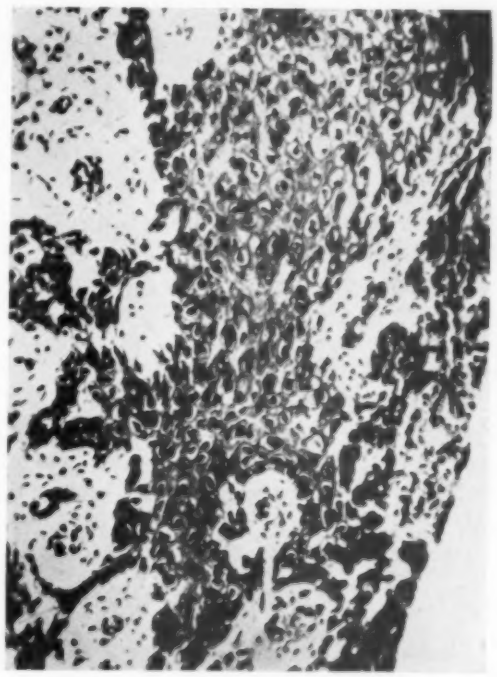

FIG. 5. Squamous cell type (× 125).

ligible roentgen-ray findings, one is amazed to find an early carcinoma of the lung. It is only in such cases that we may be able to cure those afflicted with this increasingly prevalent malady. One negative biopsy report does not exclude the possibility of carcinoma. If the endoscopist feels that the growth looks malignant, he should repeat the examination and remove more tissue for further histologic study. This should be repeated as often as feasible until a diagnosis is established. Too often the acceptance of one negative biopsy report results in the later appearance of an inoperable carcinoma.

Bronchoscopy is a great aid to the thoracic surgeon in helping to localize the lesion and in determining the operability of a given tumor. If the bronchus is fixed, it indicates that mediastinal involvement has taken place; or if the tumor extends into the trachea, surgical removal is precluded. If a suppurative lesion has occurred distal to the growth (many times these patients are sent to the hospital with a diagnosis of lung abscess), the endo-

scopist can aspirate the infected material and also dilate the bronchus in order to facilitate better drainage.

Bronchiography with the injection of iodized oil through the bronchoscope or with the catheter may aid in localizing tumors out of the range of bronchoscopic vision.

Physical Signs

Physical findings are so variable that they may simulate any type of pulmonary lesion. In our cases 97 per cent showed clinical manifestations.

Roentgenologic Studies

Roentgenologic changes were noted in approximately 99 per cent of the cases in our series. As noted by other writers, the characteristic finding was evidence of atelectasis of lung. Evidence of superimposed inflammatory reactions was noted in about 27 per cent of the cases. An absolute roentgen-ray diagnosis of carcinoma of lung cannot be made. It can be used only as a diagnostic aid.

Symptoms

The four cardinal symptoms found in our group were cough, hemoptysis, pain and dyspnea. In conjunction with these fever, chills, weight loss, wheezing and asthma were found in many of the cases.

Table XI

Symptoms	Number
Cough	43
Hemoptysis	16
Pain	30
Dyspnea	18

Cough is by far the most common symptom. At the onset in most cases it was dry and non-productive. Subsequently it often became productive of a clear, odorless, mucoid sputum. Later the sputum became blood streaked, with frank hemoptysis being noted in many cases. Those cases in which bronchial obstruction had resulted in abscess formation had a purulent sputum. Hemoptysis was usually characterized by bright red streaking of the sputum. Later in the disease the expectoration of old blood of a brownish-red color was noted. Dyspnea and wheezing are usually early symptoms of "stem-bronchus" involvement. Fever was found late in the disease when obstruction had begun to occur with formation of abscesses. This was found more frequently in "stem-bronchus" involvement. Pain, in the form of an uncomfortable sensation in the chest, is often present early in the disease, but severe pain is found late when metastases have occurred.

Treatment

Prior to the advent of thoracic surgery, the only weapons available for treatment of carcinoma of the lung were radium, roentgen-ray, and fulguration. Fulguration was usually done endoscopically but it was an unsatisfactory procedure because excision is impossible and the risk of hemorrhage is great. Many writers in years past have reported cases in which they claim to have obtained complete cures of carcinoma of the lung by this method, but from our present-day knowledge of the subject of carcinoma of the lung, one may well doubt whether they were dealing with actual carcinoma or with some inflammatory lesion. This method has been more or less completely discarded.

Radium implantations have been attempted and in some cases, if the lesion is easily accessible with the bronchoscope, one might consider this method before attempting radical surgery. This method was attempted in one of our cases for the reason that the lesion was early and the patient was 77 years of age. Thoracic surgery was out of the question; and since the lesion was early and at the same time involved the right stem bronchus, we concluded that we could give her palliative treatment in this manner. She lived for three years before the tumor began to grow rapidly with eventual fatality. In two other cases radium implantations were attempted owing to the patient's advanced age, but with scant therapeutic effect.

We have found roentgen-ray treatment to be of very little value. We are inclined to agree with Overholt, who believes that since most of these lesions are situated in main stem bronchi, one must do damage to normal tissues in order to destroy the tumor growth. In our series 15 cases were treated by deep therapy with no apparent benefit. In addition we found that it tended to produce inflammatory reactions, and to result in many systemic reactions such as loss of appetite, nausea and vomiting.

The treatment of carcinoma of the lung has finally evolved into surgical removal of the involved portion or whole lung. With the great improvement in the technic of thoracic surgery, the operative mortality has decreased in the last 10 years to an acceptable figure. Unfortunately, in our series, the cases suitable for surgical intervention were few. One left pneumonectomy was performed, and the patient is still living three years after operation. Two lobectomies were performed. One patient died six months after operation as a result of pneumonia; the other died three months after operation due to metastases, which were not demonstrable previous to operation. The important thing is to make an early diagnosis so that the case will be amenable to surgical treatment. The family physician should realize that any obscure pulmonary lesion requires thorough study until a definite diagnosis has been established. This has been well illustrated in our series of cases in that in only three cases out of 77 could surgery be considered. A great deal of progress can be made in this disease when we have succeeded in forming a capable, coöperative unit consisting of family physician, internist, roent-

genologist, bronchoscopist, surgeon, and pathologist. When this is achieved early diagnosis and successful treatment will be accomplished.

Follow-Up of Bronchoscopic Cases

All of the 77 cases herein presented died within 3 to 18 months after the diagnosis had been made except the single one that is still living three years following pneumonectomy. In a small number of these cases the diagnosis has been verified at autopsy. There are several cases living and well two years following a positive diagnosis of carcinoma of lung on tissue obtained by bronchoscopic biopsy. These have not been included in this series. The diagnosis of tissue obtained by the bronchoscope is very difficult in many instances. It is only by repeated and frequent examinations of such tissues that the pathologist will be able to make the correct decision in border-line cases.

Conclusions

1. We have presented a series of 115 primary carcinomas of the lung. Thirty-eight of these were autopsy cases. Seventy-seven were diagnosed by means of a bronchoscopic biopsy.

2. There has been a relative and an absolute increase in incidence. In our series primary lung cancer accounted for 13 per cent of the total number of carcinomas.

3. Cough, dyspnea, hemoptysis and pain are the four cardinal symptoms of carcinoma of the lung.

4. Bronchoscopic examination is by far the most important diagnostic procedure available and should be done in all cases of persistent cough whether dry or productive.

5. Of 77 cases diagnosed by bronchoscopic examination, only three cases were amenable to surgical treatment.

6. Of 77 cases, 76 were dead within three to 18 months from the time the diagnosis was made.

7. Lobectomy or pneumonectomy in suitable cases is the treatment of choice.

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THE VALUE OF SPLENECTOMY IN FELTY'S SYNDROME *

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CHAUFFARD and Ramond described the association of chronic infectious arthritis and lymphadenopathy in 1896.[1] They believed that the hemopoietic system was involved in these cases. One year later Still [2] described a deforming type of infectious arthritis in children associated with splenomegaly, lymphadenopathy, leukocytosis and anemia. Herringham [3] described a case of polyarthritis in a 15 year old boy, associated with a leukocytosis of 11,200, a color index of 0.7 (hemoglobin of 50 per cent), an enlarged spleen, and an enlarged liver. He concluded that the syndrome, described 12 years previously by Still, and atrophic arthritis were the same disease.

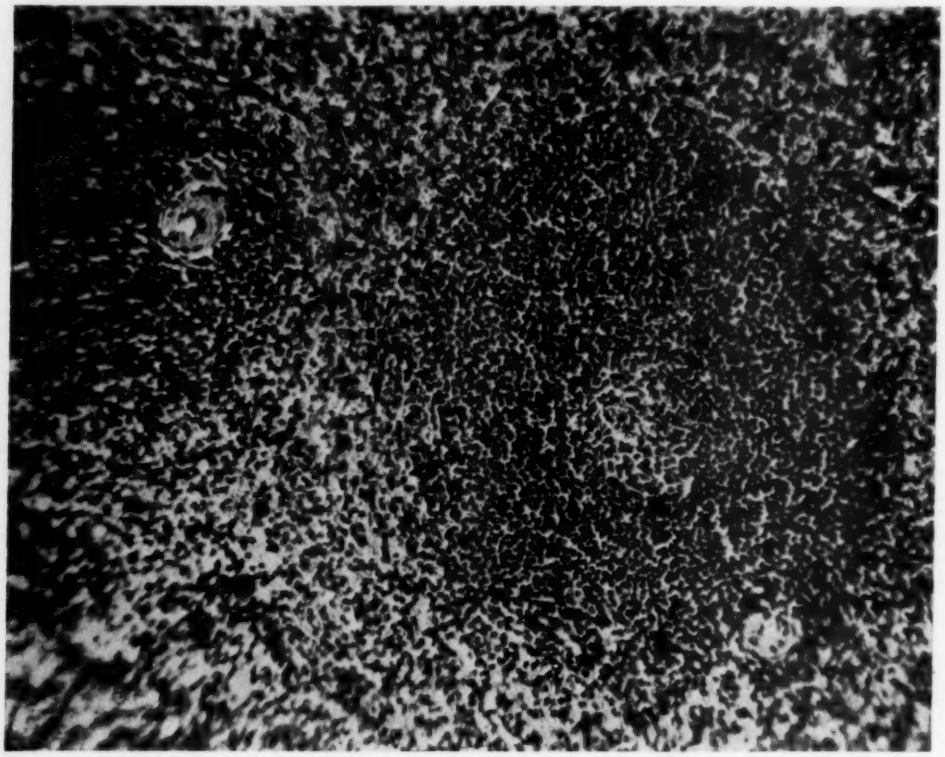

FIG. 1. Case M. Y. Low power photomicrograph of spleen showing large Malpighian corpuscles. Hematoxylin eosin. × 155.

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The gap in the bridge was closed by Felty in 1924. He [4] described a form of arthritis in the adult which was characterized by polyarthritis of the atrophic variety, fever, secondary anemia, leukopenia, splenomegaly and tachycardia. He described five cases, all of whom had arthritis of at least two years' duration. However, "in contrast to the prolonged course of the disease, and the ubiquitous distribution of pain which is the presenting symp-

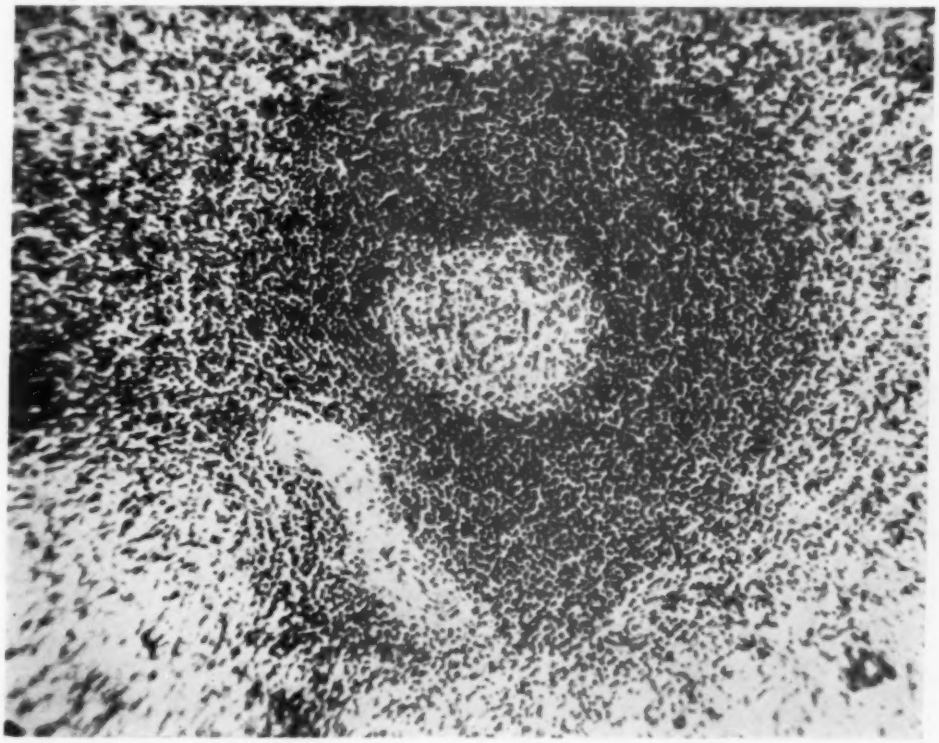

FIG. 2. Case M. Y. Low power photomicrograph shows a dilated splenic sinus, the rich cellular nature and the large germinal center of the Malpighian body. Hematoxylin eosin. × 155.

tom in all the patients, the objective findings both by physical and roentgenographic study are neither widespread nor indicative of a very damaging or destructive process." The average age of the five patients was 50 years, the range being 45 to 65. All the patients had lost considerable weight (40 to 65 pounds) since the onset of the illness. The spleen was palpably enlarged, firm and nontender in all cases. All had leukopenia, ranging from 1,000 to 4,200 leukocytes. Slight secondary anemia was present in all but one case. All had a low grade fever.

Hanrahan and Miller [5] reported the next case of this interesting syndrome eight years later. They were the first to report the beneficial effects of splenectomy in Felty's syndrome. Two years later (1934) Craven [6] de-

scribed a case of Felty's syndrome benefited by splenectomy. Alessandrini [7] described a similar case the same year, but the patient refused splenectomy. Fitz [8] reported a case in 1935.

Complete autopsy findings have been reported in two cases. In one case reported by Price and Schoenfeld [9] in 1934, the spleen weighed 510 grams. It was soft in consistency on section. It showed diffuse fibrosis and dilata-

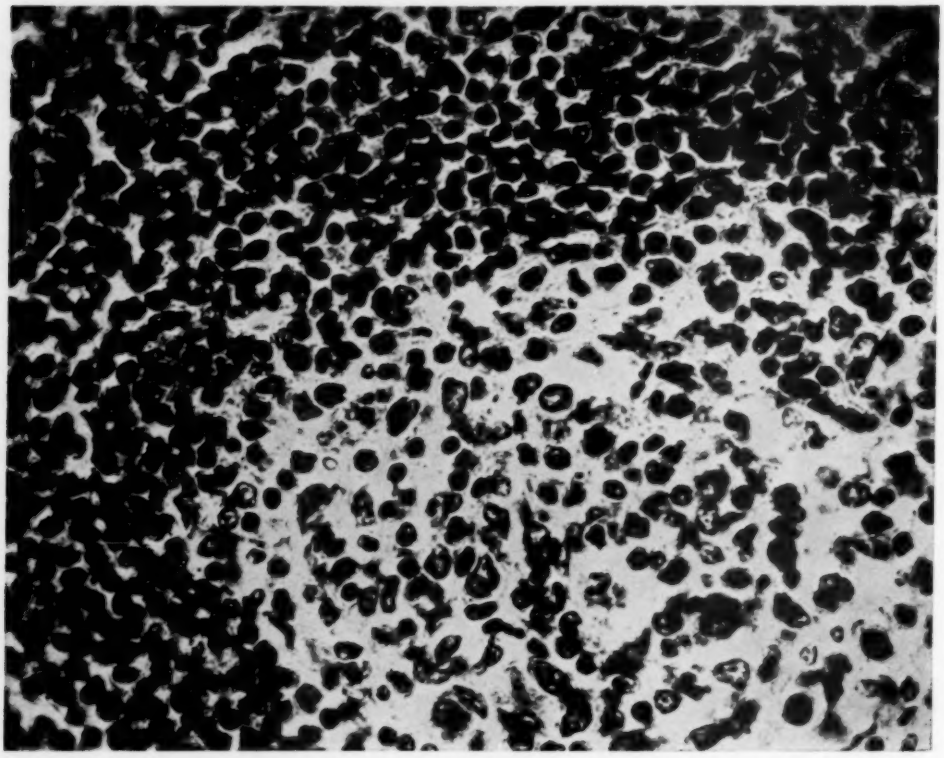

FIG. 3. Case M. Y. High power photomicrograph showing the abundance of plasma cells in the germinal center of a Malpighian body. Hematoxylin eosin. × 765.

tion of the splenic sinuses. The latter showed areas of myeloid activity with numerous plasma cells and eosinophiles. An occasional bone marrow giant cell was present. The sternal marrow showed hyperplasia with few bone marrow giant cells. Active myelosis was present throughout. In the second case reported by Williams [10] in 1936, the spleen weighed 260 grams. The capsule was smooth, gray and glistening. The pulp was dark red, firm, smooth and relatively dry. The trabeculae and Malpighian corpuscles were not very distinct. The sternal marrow showed numerous nucleated red blood cells, some stem cells and only a few granulocytes. These granulocytes were mostly myelocytes, rare polymorphonuclear leukocytes, and numerous megakaryocytes.

Curtis and Pollard [11] have recently described the pathological findings in biopsy specimens of the calf muscles of four patients with atrophic arthritis associated with leukopenia, splenomegaly, anemia and adenopathy, four cases of atrophic arthritis associated with splenomegaly without leukopenia, and four cases of atrophic arthritis associated with neither splenomegaly nor leukopenia. The pathological picture was essentially the same in all, i.e., peri-

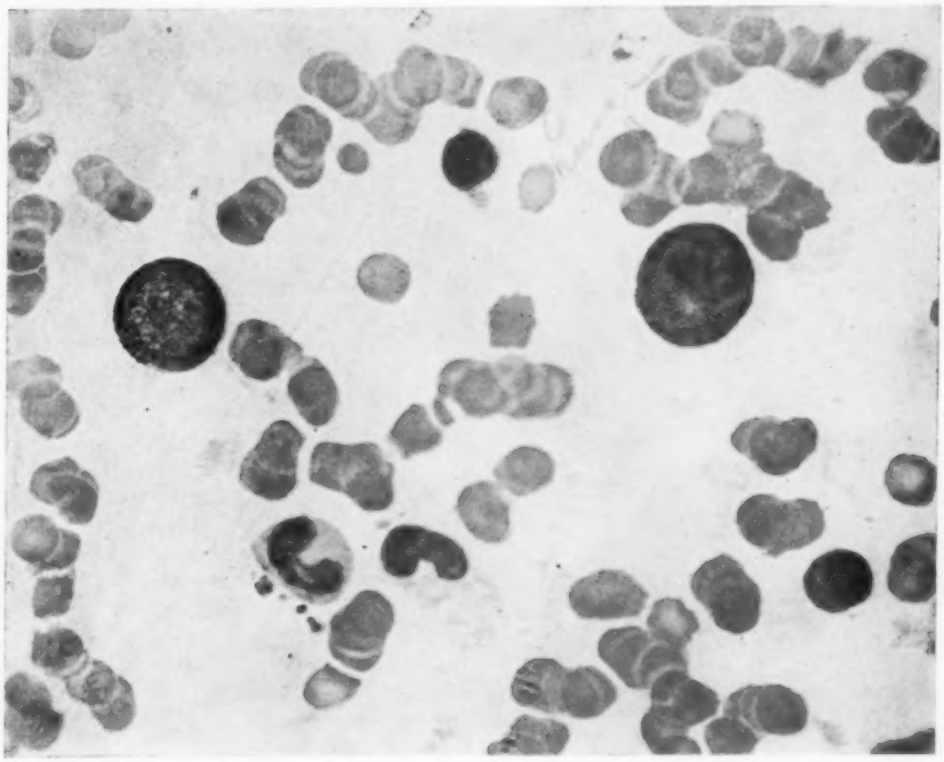

FIG. 4. Case M. Y. Sternal marrow from a white female, aged 45, with atrophic arthritis, leukopenia, secondary anemia, splenomegaly, tachycardia and low grade fever (Felty's syndrome). This photomicrograph shows two myelocytes, one metamyelocyte and one band form. Another myelocyte was seen in the same field but is not shown on this photograph. Two normoblasts are shown. The hyperplastic nature of the marrow is further suggested by the differential given in the text of this article. Giemsa's stain. × 900.

vascular round cell infiltration and an increase in the interstitial nuclei. Dawson,[12] Hench,[13] and others [14] have previously stated that Felty's syndrome is a variety of atrophic arthritis.

The leukopenia and secondary anemia characteristic of Felty's syndrome is not due to bone marrow depression. Sternal marrow studies performed on two (figures 4 and 5) of the three reported cases in this paper showed a hyperplastic marrow. Marked erythropoiesis and myelopoiesis were noted. A similar type of marrow activity was shown in the case reported by Price

and Schoenfeld.[9] The writer [15] has studied the bone marrow in 12 cases of typical atrophic arthritis (figure 6). All had a similar hyperplastic marrow. Therefore, a hyperplastic marrow is characteristic of atrophic arthritis in general and is not typical of Felty's syndrome. It probably occurs in all types of infectious disease except those cases in which the bacteria produce a bone marrow depression, as in typhoid fever, resulting in leukopenia in-

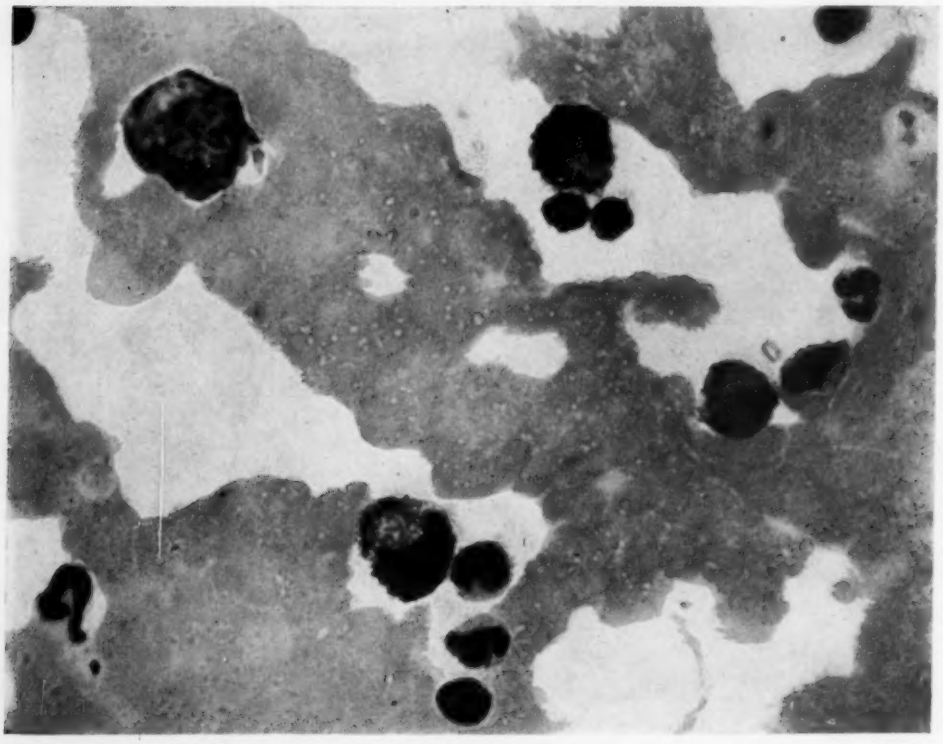

FIG. 5. Case M. B. A white female, aged 49, with atrophic arthritis, leukopenia, secondary anemia, splenomegaly, low grade fever and tachycardia (Felty's syndrome). This photomicrograph shows one premyelocyte, three myelocytes, one metamyelocyte, one band cell, and three segmented. Three normoblasts are shown. One lymphocyte is present. The hyperplastic nature of the marrow is further suggested by the differential given in the text of this article. Wright's stain. × 900.

stead of a leukocytosis. Figure 6 is a photomicrograph taken from the sternal marrow smear from a case of ordinary atrophic arthritis of at least five years' duration. It shows the typical hyperplastic picture found in atrophic arthritis and in Felty's syndrome. The differential count was as follows: myeloblasts 2 per cent, neutrophilic myelocytes 7 per cent, eosinophilic myelocytes 4 per cent, basophilic myelocytes 1 per cent, metamyelocytes 12 per cent, non-segmented 13 per cent, segmented 16 per cent, lymphocytes 20 per cent, megaloblasts 1 per cent, erythroblasts 8 per cent, normoblasts 16 per cent.

Radiographic pictures of the joints involved in Felty's syndrome are not unlike those seen in the usual type of atrophic arthritis. Decrease in the joint space, with associated articular cartilage destruction, decalcification, flexion deformities, and ankylosis are demonstrated by the radiographs shown in cases M. Y. and M. B. (figures 7, 8, and 9). Felty emphasized that the cases he described showed neither widespread physical nor roentgenographic joint destruction. However, he spoke of a two year history of arthritis, and described only five cases. No doubt a larger series of cases and a longer period of observation would have shown cases with typical joint destruction and deformities characteristic of atrophic arthritis.

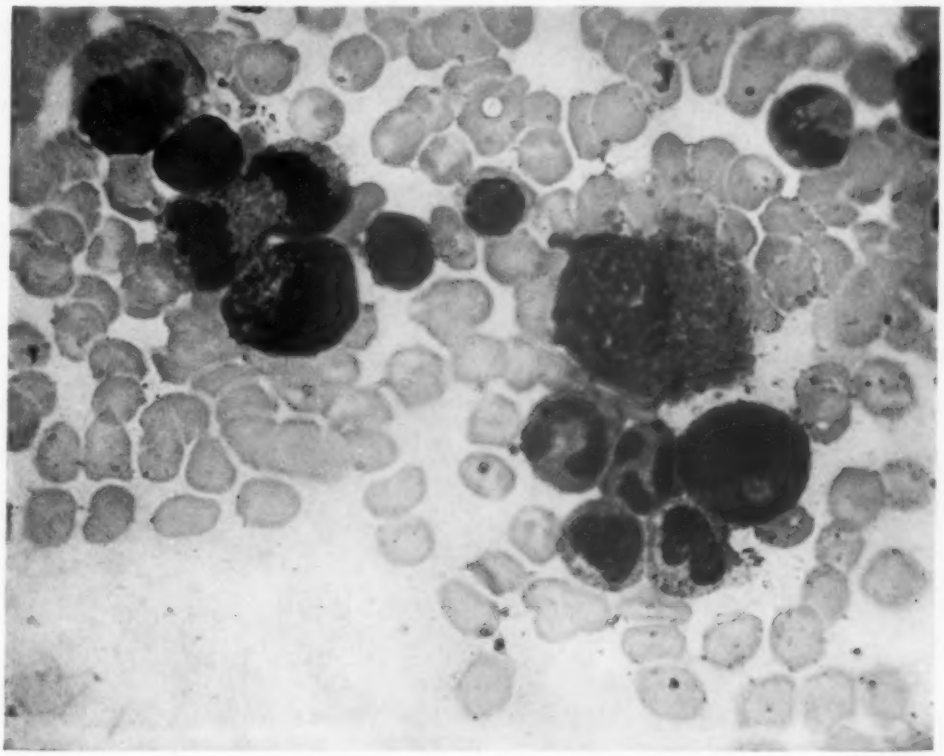

FIG. 6. Case V. Y. Sternal marrow from a white female, aged 31, with moderately advanced atrophic arthritis (arthritis vulgaris). This photomicrograph shows one premyelocyte, three myelocytes, one metamyelocyte, two band forms and two segmented indicating hyperplasia of the myeloid series. Active myelosis is shown by karyokinetic division of a myeloblast, one late erythroblast, and one normoblast present in the same field. One lymphocyte is shown. Wright's stain. × 900.

CASE REPORTS

Case M. Y. A 45-year-old white female was seen complaining of painful, swollen, stiff joints. The present illness began seven years previously, at which time pain, swelling and increase in local heat were noted in the left knee. Practically all

joints of the body became involved in gradual succession. Actual deformity of the finger and knee joints was first noted two years previously. She had not been able to walk for the preceding 18 months because of flexion deformity of the knee. She had had rare sore throats. Her teeth had been removed four years previously without benefit to the joints. Her father had crippling arthritis. She had been married 19 years and had two children living and well. She had lost about 40 pounds since the onset of the present illness.

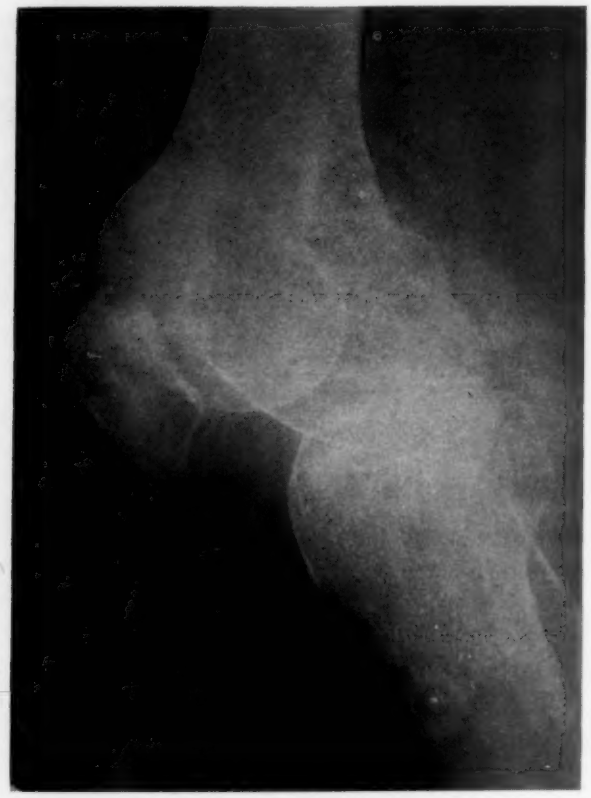

FIG. 7. Case M. Y. (Felty's syndrome). Radiographic photograph of the right knee showing the typical flexion deformity and narrowed joint space characteristic of atrophic arthritis. Lateral view. This picture was taken before orthopedic measures to straighten the joint were attempted.

The physical examination revealed a poorly nourished crippled white female whose nude weight was 96 pounds, height 5 feet, 3 inches (standard weight with clothes 138 pounds). Her oral temperature was 100.4° F., pulse rate 100 per minute, blood pressure 130 mm. Hg systolic and 90 mm. diastolic. The pupils reacted to light and accommodation. The cervical and inguinal glands were palpable. The neck, lungs, and heart were negative. The spleen was barely palpable. The cervix was badly lacerated, and the rectal examination was negative. There was marked deformity of the fingers of the left hand and less deformity of the fingers of the right hand. Most of the interphalangeal joints were subluxated. Flexion deformity was present in the left wrist. This joint was swollen, very tender and warm. Slight

flexion deformity was present in both elbows. Increase in local heat was present in both these joints. Pain on motion and complete lack of abduction were present in both shoulders. There was no motion in either knee, and both knees had a right angle deformity. Swelling and increased local heat were present in both these joints. There was practically no motion in the ankles. The anterior arches were flat.

The laboratory examination was of unusual interest due to the persistent leukopenia which responded to no method of therapy except persistent blood transfusions.

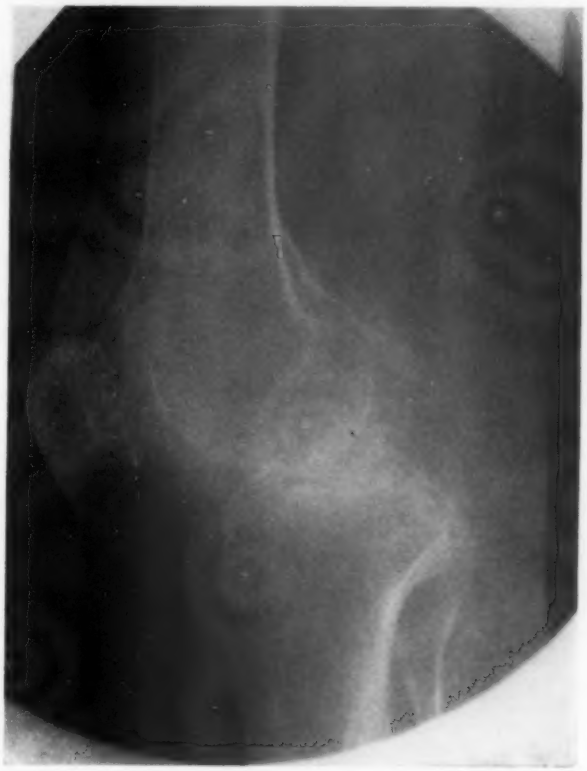

FIG. 8. Case M. Y. (Felty's syndrome). Radiographic photograph of the right knee after it was straightened by plaster application. The general health improvement that followed splenectomy permitted this procedure to be carried out. Some subluxation is present.

The blood transfusions acted as temporary agents in raising the white blood count and improving the secondary anemia. Reduced iron, liver, and yellow bone marrow all resulted in no improvement. Figure 10 reveals the effect of all these various agents on the white blood count, red blood cells, hemoglobin and platelets. Wassermann and complement fixation tests for the gonococcus were negative. The blood uric acid was 2.80 mg. per 100 c.c. of blood. Icterus index was 5. The reticulocyte count varied from 0.1 per cent to 7.1 per cent. Serum calcium was 9 mg., and serum phosphorus was 4.1 mg. Sternal bone marrow revealed the following interesting blood picture: 7 per cent myeloblasts, 9 per cent premyelocytes, 18 per cent neutrophilic myelocytes, 1 per cent eosinophilic myelocytes, 1 per cent basophilic myelocytes, 7 per cent metamyelocytes, 8 per cent band forms, 12 per cent segmented, 1 per cent eosinophilic segmented, 8 per cent large lymphocytes, 6 per cent small lymphocytes,

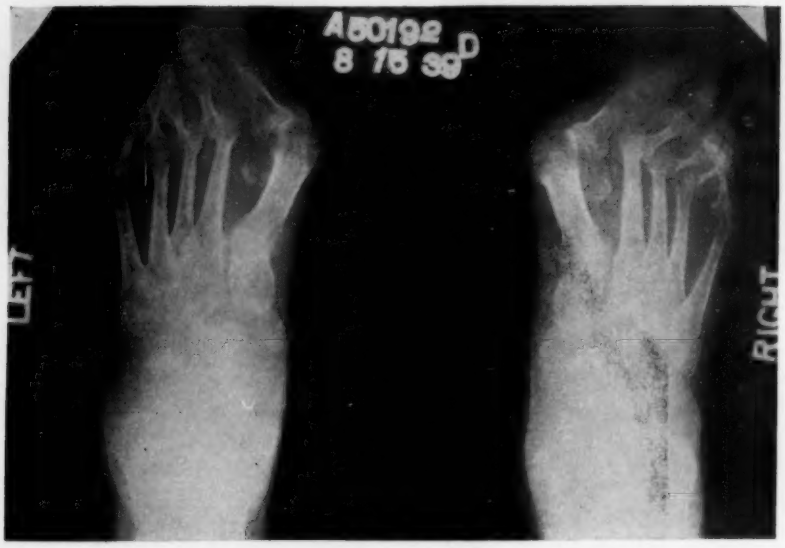

FIG. 9. Case M. B. (Felty's syndrome). Radiographic photographs of the feet showing the typical joint destruction characteristic of advanced atrophic arthritis.

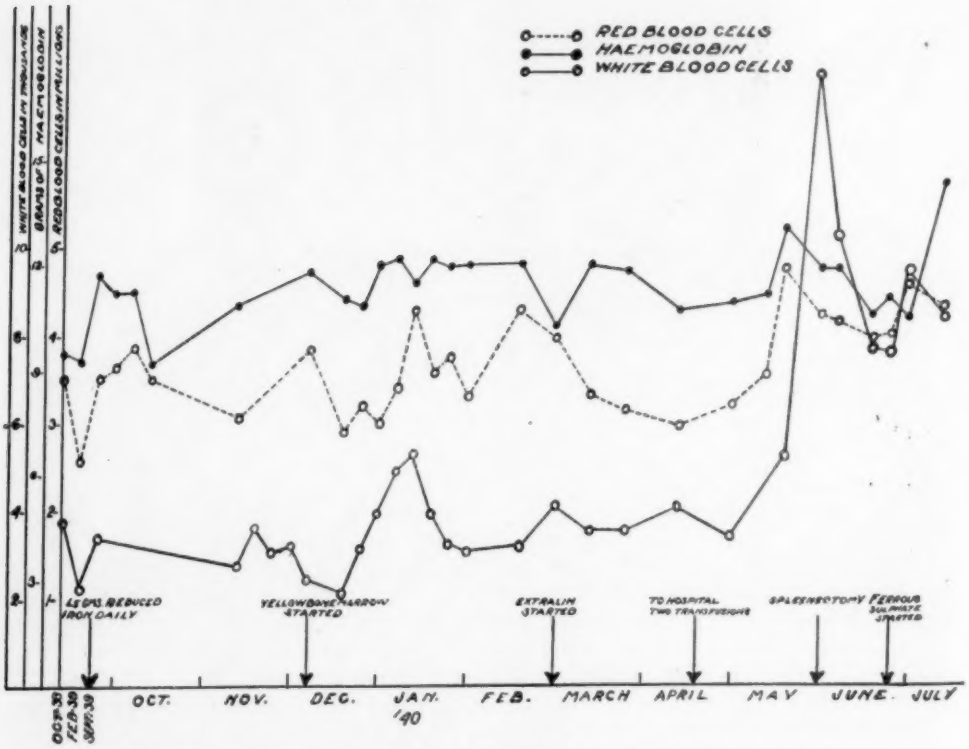

FIG. 10. Case M. Y. Effect of various drugs on blood regeneration.

3 per cent megaloblasts, 9 per cent erythroblasts, 2 per cent monocytes, 2 per cent plasma cells.

Since the bone marrow was found to be able to produce its cells in abundant quantities, it seemed plausible that the spleen might act as a barrier in not permitting the peripheral blood to receive these cells in sufficient quantities. A splenectomy seemed to be a rational procedure. The marked and continued improvement in the blood picture resulting from the splenectomy is shown in figure 10.

The histologic picture of the removed spleen is shown in figures 1 and 2. The Malpighian bodies were quite large and showed large germinal centers. The latter exhibited an abundance of plasma cells. The pathologist unfortunately failed to give a gross description of the spleen. The surgeon who removed the spleen stated that it was about three times normal size (14 by 9 by 4.5 cm.).

No noticeable improvement in the arthritis occurred as a direct result of the splenectomy. However, the general clinical improvement permitted orthopedic measures to be carried out successfully. The radiographic photographs (figure 7) showed the flexion deformity present before the plaster casts were applied, and the radiographic picture (figure 8) showed the end result of such procedure. The patient had about 10° motion in both knees; they were straight, but there was some subluxation of the joints present. Her fever had disappeared, but a tachycardia of 100 to 110 continued. She had gained in weight, appetite, and strength.

Liver extract and yellow bone marrow failed to improve the peripheral blood picture. After all these methods failed a study of the sternal bone marrow was made. It showed a hyperplastic bone marrow as follows:

Myeloblasts	7
Premyelocytes	9
Myelocyte neutrophiles	8
Myelocyte eosinophiles	1
Myelocyte basophiles	1
Juveniles	7
Band forms	8
Segmented neutrophiles	12
Segmented eosinophiles	1
Large lymphocytes	8
Small lymphocytes	6
Megaloblasts	3
Erythroblasts	9
Monocytes	2
Plasma cells	2

With such evidence that the bone marrow was not aplastic and could deliver cells, why did all recognized methods of therapy fail to secure improvement of the peripheral blood? Where was the barrier between the hemopoietic centers and the peripheral blood? Was the spleen acting as a barrier? The latter conclusion seemed plausible. Splenectomy was carried out after bringing the blood up nearly to a normal level with transfusions. There was decided improvement of the patient's blood and general condition immediately following splenectomy. However, within a period of three weeks after the splenectomy, a gradual decline was observed in the blood picture and in the patient's general condition. Anorexia was a most difficult symptom to combat. The patient developed a peculiar depressed mental attitude. Frequent cheerful conversations and the forcing of highly nutritious foods rich in vitamins overcame this condition.

The above decline in the patient's condition associated with marked anorexia calls for a careful restudy of the previously reported cases showing improvement after splenectomy.

The follow-up on the two cases of Felty's syndrome [5, 6] reveals that both cases died a comparatively short time after operation. Craven's [6] case died 14 months after operation of general inanition and a terminal bronchopneumonia. Hanrahan and Miller's [5] case died 18 months after operation. The cause of death was not given. Both of these end results were reported by Fitz.[8] The case reported in this paper also showed signs of general inanition resulting from her marked anorexia. However, she maintained a normal white blood count and the secondary anemia responded to iron therapy. The low grade fever disappeared following operation. No method of therapy had secured these results before operation.

Case G. P. A 39-year-old white female complained of painful swollen joints. The illness began 24 years previously, with painful swelling of both wrists, both ankles and of all proximal interphalangeal joints. An acute exacerbation of the arthritis occurred four years later. The patient has remained essentially unchanged since this last flareup. She had had scarlet fever at eight years of age, and had had only an occasional sore throat. She had had herpes at 20. Her Wassermann reaction was negative in 1932 but four plus in 1934. Her father had deforming arthritis. She had three children living and well. Her husband and all children had negative serological tests for syphilis.

The physical examination showed a well developed, well nourished, intelligent white female whose nude weight was 132 lbs., temperature 97.6° F., pulse rate 100 per minute, and blood pressure 130 mm. Hg systolic and 96 mm. diastolic. Examination of the head was negative. The teeth and tonsils had been removed. Cervical and inguinal adenopathy was present. Examination of the lungs and heart was negative. Abdominal examination revealed an enlarged, non-tender, firm spleen which was felt two fingers' breadth below the costal margin. Rectal and vaginal examinations were negative. There was fusiform swelling of the proximal interphalangeal joints characteristic of atrophic arthritis. The capsules of both knees and both ankle joints were moderately thickened. Increase in local heat and tenderness was present over the left shoulder joint. No deformities were present.

A communication from Dr. Richard P. Stetson on June 6, 1940, revealed the following interesting blood studies. These studies were done September 6, 1932, at least two years before the positive serological test for syphilis was discovered.

"Mrs. G. P. has asked me to write you regarding her white blood count when I saw her in 1932. I have only one count recorded. This was on September 6 of that year. She had a red blood count of 5,150,000 with a hemoglobin of 80 per cent. The appearance of the cells was slightly abnormal with slight variation in size and shape; no true microcytes or macrocytes were seen but a rare cell was smaller and a few seemed larger than the average; there were a few elongated and a rare tailed cell and a moderate degree of achromia in most cells, there was slight polychromatophilia in an occasional cell. Although the count and hemoglobin were normal the appearance of the cells was that of a mild secondary anemia. The platelets were normal. As for the white blood count, the total number was 3,300 with 53 per cent polymorphonuclear neutrophiles, 2 per cent eosinophiles, 29 per cent normal lymphocytes, 8 per cent large lymphocytes, 7 per cent monocytes and 1 per cent unclassified cell, probably an atypical lymphocyte." She was given alternate doses of mapharsen and bismuth until January of 1940, at which time the Wassermann reaction was reversed.

The laboratory studies are given in figure 11. Note the effect of liver extract on the leukocyte count. The leukopenia before the syphilitic infection and the persistent leukopenia for eight years after stopping all arthritic therapy indicate no rela-

tionship between the syphilis and the blood picture. The atrophic arthritis, tachycardia, splenomegaly, leukopenia, secondary anemia, and lymphadenopathy are consistent with a diagnosis of Felty's syndrome.

Course: The arthritis entirely subsided under treatment with hemolytic streptococcal vaccine. She was given nine capsules of extralin daily beginning March 1, 1940, with slight improvement of the leukopenia.

Case M. B. (3). A 49-year-old white female was seen complaining of painful swollen joints. The present illness had begun 10 years previously at which time pain

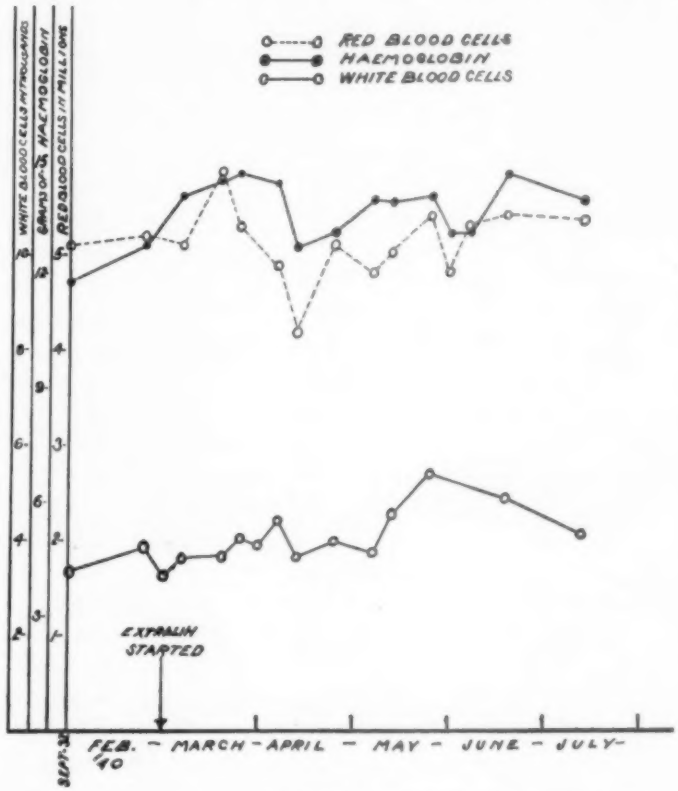

FIG. 11. Case G. P. Effect of extralin on blood regeneration.

was noted in the balls of the feet upon walking. Swelling was later noted in this area. The knees, all the finger joints, wrists, elbows and ankles have progressively become swollen, painful and warm to the touch. Marked pain on motion soon became evident in the shoulders and hips. The joints had been made much worse by two exacerbations, one of which had occurred seven years previously and another three years previously. The latter exacerbation was preceded by erysipelas. She had lost considerably in weight since the onset of the arthritis. The exact amount was unknown.

The physical examination revealed an undernourished white female lying more or less helpless in bed with typical deformities of the joints characteristic of advanced atrophic arthritis. Temperature was 99° F., pulse rate 86 per minute, blood pressure 124 mm. Hg systolic and 70 mm. diastolic. The pupils reacted to light and accommodation. All the teeth were out. The tonsils were small and appeared innocent.

Examination of the neck, lungs and heart was negative. The spleen was barely palpable. It was firm and nontender. The finger joints were deformed in the most grotesque manner. Most of the phalanges dangled from their joints. Flexion deformity was present at the metacarpophalangeal and wrist joints. Ulnar deviation was marked. The elbows were fixed in flexion. Marked abduction deformity of the shoulders was present. The hips were in flexion deformity with only about 20° motion present; 30° flexion deformity was present in both knees. There was slight shortening of the Achilles tendon of both heels. No increased local heat or marked

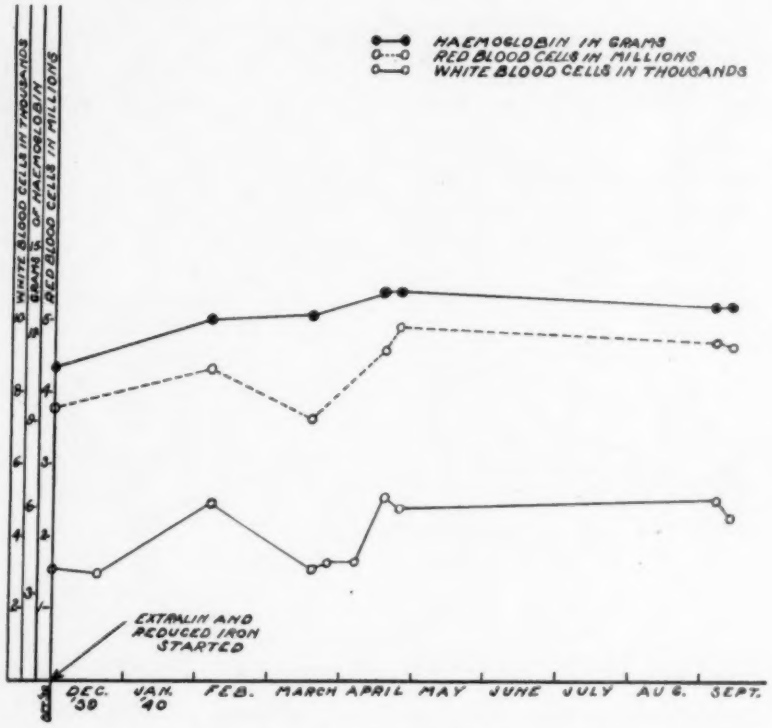

FIG. 12. Case M. B. Effect of extralin and iron on blood regeneration.

soft tissue swelling was present. Hard fibrous nodules from one to three cm. in diameter were noted along the ulnar border of the elbows.

The most interesting laboratory finding was the leukopenia. This was associated with a mild secondary anemia. The patient was treated by bed rest, nine capsules of extralin and 1.5 grams of reduced iron daily. General muscle massage, active and passive exercises and moist heat were employed. Hemolytic streptococcal vaccine was given intravenously. The blood findings and their response to therapy are shown in figure 12.

The typical findings of atrophic arthritis, the leukopenia, splenomegaly, and secondary anemia, along with a marked weight loss, establish the Felty syndrome. Both the leukopenia and the secondary anemia responded to liver and iron therapy. Although it was impossible to weigh the patient because of her deformities, she gained considerably in weight. There has been little change as regards joint improvement.

Sternal marrow showed a hyperplastic picture (figure 5). The differential count was as follows: Neutrophilic myelocytes 10 per cent, eosinophilic myelocytes 5 per cent, metamyelocytes 7 per cent, band forms 10 per cent, segmented 18 per cent, lymphocytes 20 per cent, eosinophilic segmented 5 per cent, megaloblasts 4 per cent, erythroblasts 4 per cent, normoblasts 17 per cent.

In the therapy of this interesting syndrome, one should first remember that the disease is a chronic constitutional one with all the signs and symptoms of chronic infection. Its general management should be no different from that of tuberculosis. Absolute bed rest, a highly nourishing diet rich in vitamins, and mental as well as physical relaxation are required. A careful study of the peripheral blood should be made on several occasions to rule out aleukemic leukemia and aplastic anemia. A careful history for undulant fever, agglutination tests, blood cultures and skin tests should rule out *Brucella abortus* infections. Tuberculosis must be ruled out. The arthritis per se rules out Banti's disease. Most important, bone marrow studies should be done to determine the degree of activity or inactivity of the marrow. If inactivity is present splenectomy could not possibly be of value. Bone marrow stimulants such as liver, yellow bone marrow, pentnucleotide, etc., should be tried. If the marrow is hyperplastic and all other known methods have failed, splenectomy is in order.

Three cases of atrophic arthritis associated with a syndrome described by Felty are presented. The leukopenia and secondary anemia were successfully controlled in two cases by giving liver extract or liver extract and iron. All efforts to improve the peripheral blood picture failed in one case. Splenectomy proved of value in this latter case. Bone marrow studies in two of these patients revealed a hyperplastic marrow. The deficiency of cells in the circulating blood seems not to depend upon inadequate formation by the marrow, but upon some barrier to their entrance into the circulation. The most probable barrier is the spleen as demonstrated by the improvement noticed in the case reported in this paper and the cases previously reported in the literature.

Splenectomy should be done only after all conservative measures fail. One patient reported in this paper had a leukopenia for eight years without apparent ill effect. Her blood picture either improved spontaneously or else the liver extract was effective therapeutically. Improvement in the blood picture after splenectomy has been associated with general clinical improvement. It has not directly altered the course of the arthritis.

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PROSTATITIS—A CAUSE OF ACUTE OR RECURRENT ABDOMINAL PAIN *

By Harry Freund, M.D., *Brooklyn, New York*

Abdominal pain, when acute, is a symptom which frequently presents a baffling diagnostic problem. If the pain is chronic, this problem often becomes even more perplexing. In a series of six patients coming under my observation, each presenting abdominal pain as his major complaint, the usual causes for such pain were not apparently operative in any case. However, a thorough physical examination showed each to have an inflammatory process residing in the prostate. This finding was confirmed by the presence of definite pus in the expressed secretions of the gland, and, in each instance, no other objective findings were noted which were considered as relevant to the chief complaint. Before conclusively inculpating the prostate as a source for the subjective sensation of pain in the abdomen, I shall outline briefly the history and clinical course of these patients.

Case Reports

Case 1. A white male, aged 25, unmarried, was first examined in July 1936. His chief complaint was pain in the right lower quadrant of the abdomen of four months' duration. Associated symptoms included a continuous burning sensation at the tip of the penis for two weeks and occasional fleeting pains in the rectum and coccygeal region for many months. Previous observation and examination indicated the probable diagnosis was either a strain of the abdominal musculature, or chronic appendicitis. The patient was advised to wear an abdominal supporting belt which he did for two months with no relief. The patient denied venereal disease by name and symptom. He had had no previous sexual experience but admitted to frequent masturbation over a period of years. Physical examination disclosed normal heart and lungs. Palpation of the abdomen disclosed no spasticity or tenderness and no masses or enlarged organs. Examination of the prostate showed it to be slightly enlarged and boggy and to be distinctly tender especially in the right lateral lobe. When pressure was exerted over this more tender area the patient experienced abdominal pain identical in character and location to that felt subjectively. Microscopic examination of the prostatic smear showed many large clumps of pus cells. No gonococci were found. Local treatment including massage, diathermy, and instillations of silver nitrate solution into the posterior urethra effected complete relief from all symptoms. A recent examination of the patient, two years after treatment, showed him to be free from all signs and symptoms previously noted.

Case 2. A white male, aged 70, complained of constantly recurring and frequently severe pain in the right lower quadrant of the abdomen, which occasionally radiated to the left lower quadrant. This pain had begun to trouble him 10 years prior to this examination, and was constantly increasing in frequency and severity. Within the last three years symptoms of prostatic obstruction also began to appear. These included slowing of the stream, difficulty in starting the flow, dribbling, etc. Within the past two years, he began to experience angina pectoris and symptoms indi-

* Received for publication April 29, 1940.

cative of cardiac insufficiency. When the pain had first presented itself, the patient was advised that a hernioplasty for the cure of a longstanding hernia might effect relief of his abdominal pain. The operation was done, but it failed to accomplish this result. Three years afterward a hemorrhoidectomy was performed on the assumption that the hemorrhoids and concomitant constipation might be the responsible factor. Physical examination showed an elderly white male appearing chronically ill. Lungs were emphysematous, and contained bibasal râles. The heart was considerably enlarged, especially to the left. The heart sounds were forceful with a long blowing systolic murmur present at the apex. Blood pressure was 240 mm. Hg systolic and 140 mm. diastolic. The liver was enlarged to two fingers' breadth below the costal margin and had a smooth tender edge. The prostate was distinctly enlarged and contained many nodules. It was very tender, especially in the right lateral lobe, and pressure over this area elicited exactly the same type of pain complained of by the patient. These findings were entirely corroborated by a competent urologist, Dr. Perry Katzen of Brooklyn, whom I asked to confirm my own observations. Prostatectomy was subsequently performed but the cardiac status was so poor that the patient did not survive the procedure.

Case 3. A white male of 23 presented himself in March 1938 complaining of severe pain in the right lower quadrant of the abdomen associated with vomiting and fever of one day's duration. Associated symptoms included burning and frequency of urination. He admitted illicit sexual contact two days prior to the onset of his illness. He had no previous illness of consequence except for an untreated gonococcal urethritis at 19. Physical examination revealed the patient to be acutely ill. Temperature was 101° F., the pulse rate 100 per minute. The throat, heart and lungs were negative. There was marked tenderness in the right lower quadrant and suprapubic region, with considerable muscle spasm of involuntary nature. Rectal examination showed no tenderness in the region of the appendix or either iliac fossa. The prostate was moderately swollen and exquisitely tender. A smear of the gently expressed secretions of the gland contained pus and many gram-negative intracellular diplococci. The following day a fully developed urethritis was present.

Cases 4, 5, and 6. I have grouped the accounts of these cases because each exhibited strikingly similar histories and physical findings. Ages were 39, 31, and 25 respectively. All were married and as a rule practiced coitus interruptus. Cases 4 and 5 admitted also a previous gonococcal infection. The major presenting complaint in each was chronic recurrent pain in the abdomen. In cases 5 and 6 a probable diagnosis of chronic appendicitis had been made and operation recommended. All showed a tender prostate, and the presence of infection was confirmed by laboratory examination. Conservative local therapy directed toward the prostate achieved relief of signs and symptoms.

Analysis of Cases

This series of patients all presented a number of symptoms and signs which constitute a fairly definite clinical syndrome. All complained of abdominal pain, principally of a chronic variety, and most frequently located in the right lower quadrant. In each instance, also, the prostate was tender on palpation. Expressed prostatic secretions uniformly showed pus. When the patient first presented himself the complaint of pain had been present in all but one case for from one to 10 years. In three cases the diagnosis of chronic appendicitis had been seriously entertained. Case 2 was subjected first to a hernioplasty and subsequently to a hemorrhoidectomy, primarily for relief of the pain in the abdomen, but no relief of the presenting symp-

tom was achieved. Case 3 showed enough objective findings to indicate strongly the necessity for a possible appendectomy. The etiologic factor determining the production of the prostatitis varied, being masturbation in case 1, prostatic hypertrophy and infection in case 2, a recurrent gonococcal urethritis in case 3, and coitus interruptus in the remainder. Masturbation and coitus interruptus have for some time been recognized as potent causative agents in the development of chronic prostatitis. Dr. Hugh Young, in Nelson's Loose-leaf Surgery, inculpates masturbation as such an etiologic agent. It is most significant and worthy of emphasis that pressure over the tender portion of the prostate reproduced exactly the pain complained of by the patient. This finding led me to the natural conclusion that prostatic disease could simulate chronic painful intra-abdominal disease. I was prompted, therefore, to confirm my findings by consultation with a competent urologist. This I did as stated above in the history of case 2. Dr. Katzen stated at the time that he had no previous knowledge of the existence of any relationship between pain in the abdomen and prostatic disease. It is not difficult to understand why such cases do not as a rule come under the care of the urologist. The major complaint being abdominal pain, the patient would naturally present himself first to his family physician or to a surgeon or gastroenterologist. Since a relationship between abdominal pain and prostatic disease has not been particularly stressed in the past, it is possible that the prostate as an offending agent may be occasionally overlooked.

Comment

Ever since the work of Head, whose brilliant investigations in the field of subjective pain sensation have led to a better fundamental understanding of the problem, we have become more and more accustomed to the idea that "Pain is not where you find it." The theories formulated by Head, relating to the vagaries and habits of the human nervous system in appreciating painful sensations, have uncovered a whole new approach to the diagnosis and treatment of organic disease. A careful perusal of the more recent texts on the subject of urology failed in most cases to reveal any mention of the relationship between abdominal pain and prostatic disease which I have here tried to establish. Only Wesson [1] has directly mentioned such a relationship, and even he emphasized the seminal vesicles rather than the prostate as the source of pain. However, it is obvious that with a common innervation for both structures it would be possible to assume the prostate at fault occasionally as well as the seminal vesicles. It is common knowledge that disease in the prostate may produce pain in the small of the back, the buttocks, the thighs, the scrotum, the groins, and even the leg or foot. Unfortunately, the exact innervation of the prostate and other parts of the lower genitourinary tract is not as yet known, but it is believed that the pelvic nerve provides the most important pathway for both afferent and efferent impulses for this entire region, including the bladder, seminal vesicles, prostate and

urethra. With the knowledge gained from the many studies of referred pain it is not difficult to understand how pain impulses might readily be referred over sensory pathways at higher levels in the cord, than might be anticipated, so that a relatively wide range of abdominal surface areas might conceivably be affected. A similar type pain in unusual or unexpected areas is met with in the case of disease of other organs. As Libman in particular has pointed out, this is true of pain of cardiac origin. The pain of angina and coronary spasm not uncommonly radiates to such regions as the teeth, ear and leg. Suffice it, therefore, again to emphasize the vagaries of pain in the abdomen, and to suggest that when a cause for such pain is not obvious in the male patient a thorough examination of the prostate be included.

Summary

1. A group of cases is presented exhibiting abdominal pain in which a diseased prostate was found to be the source of such pain.

2. A plea is made for the examination of the prostate in all male patients, especially in those exhibiting abdominal pain as a symptom.

3. It is suggested that suspected but not proved cases of chronic appendicitis in males be investigated as possible cases of chronic prostatitis to determine whether or not such disease might possibly be masquerading as appendicitis.

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EOSINOPHILIA IN FATAL ASTHMA; STUDIES OF BONE MARROW AND MYOCARDIUM *

By Francis H. Chafee, M.D., F.A.C.P., John R. Ross, M.D., and E. Mansfield Gunn, M.D., *Providence, Rhode Island*

The finding of marked eosinophilic infiltration in the bone marrow and heart of a man who had suddenly died in an asthmatic paroxysm stimulated us to review the literature and previous autopsies on cases of asthma at the Rhode Island Hospital in order to obtain more information relative to this condition.

The literature lists few autopsied cases. Coca [1] in 1931 summarized them and found 33 for his discussion. Lamson and Butt [2] in 1937 brought the series up to date, finding 50 cases and adding 48 of their own. Fowler [3] in that same year reported two cases, and Thieme and Sheldon [4] in 1938 reported seven in which death could be attributed to the asthmatic paroxysm. We have reviewed all of these reports.

In addition, the autopsy records of the Rhode Island Hospital from January 1, 1929 to February 8, 1940 were searched for cases of fatal asthma. Of 3,241 autopsies performed during those years, we are reporting six in which there was a definite asthmatic history. Bone marrow from the upper third of the shaft of the humerus and from the lumbar vertebra was available for study in four of the six cases. One autopsy is deficient in material for extensive study, but is included because of the cardiac pathologic lesions found.

Only the pertinent material will be given, and the case which led us to make this study will be presented first.

Case Reports

Case 1. W. W., white male, aged *27*, was admitted February *2*, 1940.

History: The family history revealed twin cousins with asthma.[9] The past history was irrelevant except for an attack of rheumatic fever four years previously, at which time he had spent two months in bed. He had had a tonsillectomy in childhood. He had always been prone to obesity and had always some shortness of breath attributed to it. About the age of seven he had his first attack of wheezing. According to his family physician, no other attacks occurred until November 1939 at the age of *27*. A chronic nasal obstruction was relieved in January 1939 by the removal of several nasal polyps. Roentgenograms in May 1939 revealed ethmoidal disease, and these sinuses were curetted in July of that year. Asthma, according to the patient, really began in October 1939. The attacks were mild at first, gradually increasing in duration and severity. For the fortnight before entry attacks were continuous, with medication giving only transient relief. No causative factors could

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be determined. Skin tests in January 1940 showed questionable reactions only to rice, timothy and cotton seed.

Physical Examination: On the day of admission the temperature was 99.6° F., the pulse 132, respirations 35, and the blood pressure 115 mm. Hg systolic and 60 mm. diastolic. The patient was an obese white male weighing 240 pounds, sitting up in

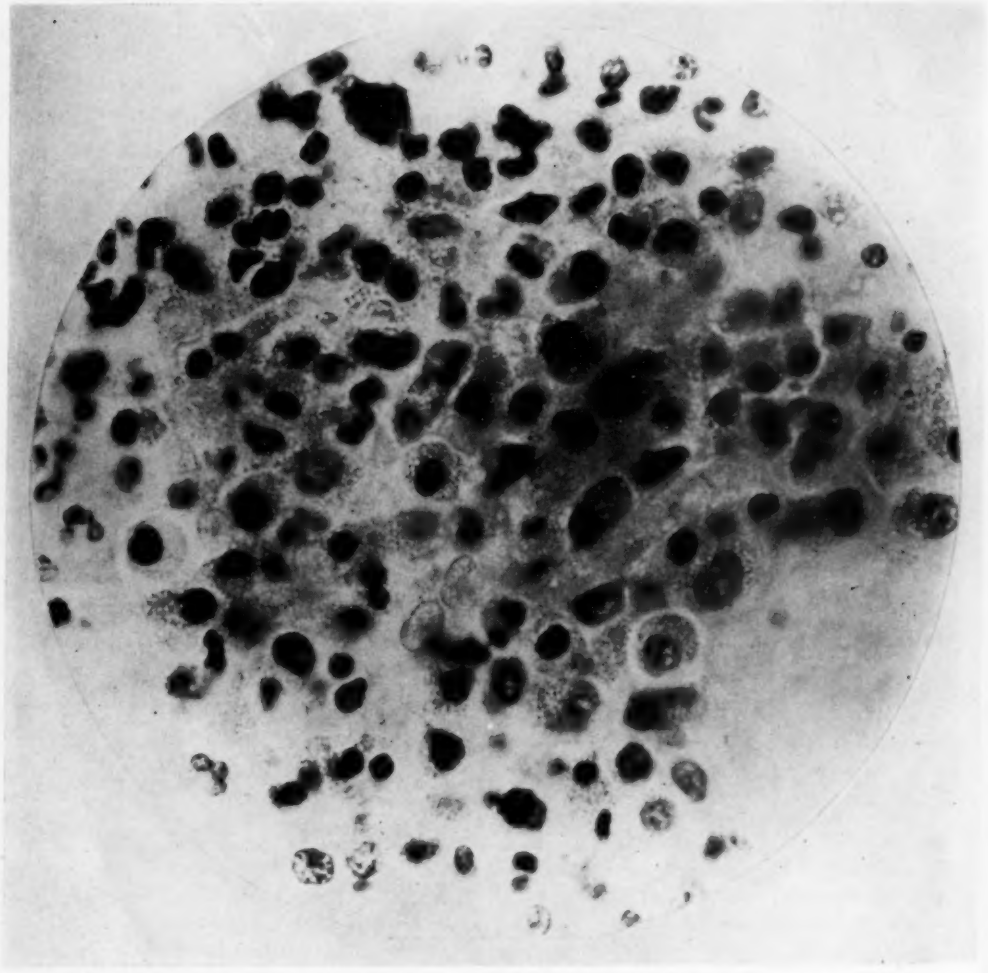

FIG. 1. Bone marrow, showing many eosinophilic polymorphonuclear leukocytes.

bed with mild respiratory difficulty. No cyanosis was noted. The nose was partially blocked. The heart was not enlarged to percussion. The sounds were distant with no audible murmurs. Characteristic asthmatic râles were heard throughout both lung fields.

Laboratory Findings: Roentgenogram of the chest on February 3 showed mottling irregularly scattered through both sides suggestive of bronchopneumonic consolidation. Electrocardiogram showed a rate of 104 with normal conduction time. There was a small S-wave in Lead I, a deep S in Leads II and III, and the T-waves were not remarkable. The S T segment was deep and a definite left axis deviation was noted.

The record was interpreted as being abnormal but significant of no special type of heart disease. The urine and Wassermann reaction were negative. The white blood count was 8100. The differential count showed neutrophilic leukocytes 66 per cent, lymphocytes 20 per cent, and eosinophilic leukocytes 14 per cent. The blood urea nitrogen was 6.3 mg. per cent and the blood glucose 74 mg. per cent.

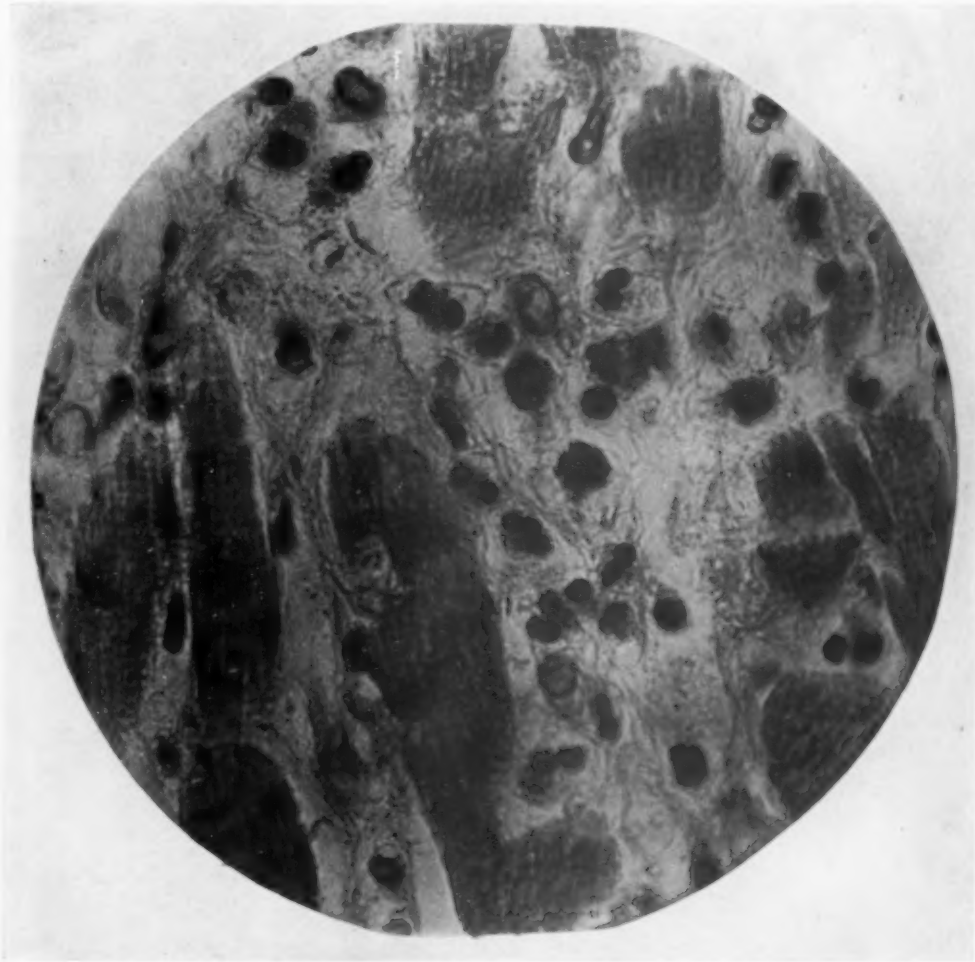

FIG. 2. Myocardium showing infiltration of the intermuscular spaces by eosinophilic polymorphonuclear leukocytes.

Course: Under adrenalin-in-oil there was slight improvement until the sixth hospital day. That morning a severe attack commenced. The usual therapy of aminophyllin, adrenalin, and oxygen gave no improvement. During that night, his temperature being 99.8 F., and pulse 180, he was given paraldehyde and other sedatives with no effect. Pantopon, gr. ⅙, administered early in the morning six hours after the last preceding medication, resulted in the first sign of improvement. He was found dead in bed two hours later.

Postmortem Examination: Adiposity was especially prominent about the shoulder and pelvic girdles.

The heart weighed 450 gm. The wall of the right ventricle averaged 15 mm. in thickness, the wall of the left ventricle 10 mm. There were no changes in the coronary arteries. It was in the histological examination of the myocardium that most interesting findings were revealed. The myocardial fibers in many areas had lost their striations and in places had assumed a pinkish homogeneous stain. In many of these

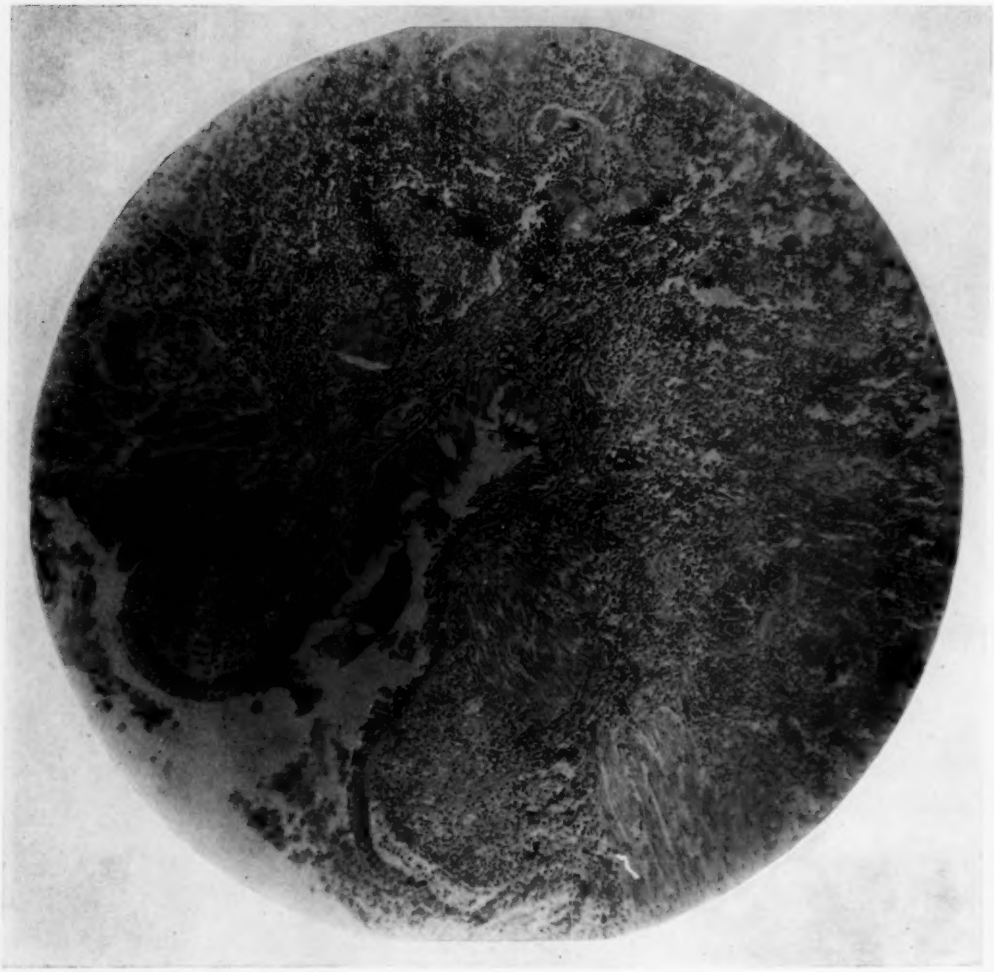

FIG. 3. Bronchus showing squamous metaplasia of lining epithelium, thickened basement membrane, chronic bronchitis, smooth muscle, and a few mucous glands.

areas of degeneration there was a massive infiltration of eosinophilic polymorphonuclear leukocytes with only a few lymphocytes and plasma cells. The eosinophilic polymorphonuclear leukocytes were not limited in distribution to areas of necrosis, but were also evident in the intermuscular and perivascular spaces, as well as the subepicardial fat. Deposits of fibrin were occasionally found in some of the intermuscular spaces. No actual fibrosis was present. In a few instances near small blood vessels and in the intermuscular spaces there were small foci of necrosis about which were collections of lymphocytes, plasma cells, and large mononuclear cells. There were

no eosinophilic polymorphonuclear leukocytes in these accumulations, nor were any giant cells seen. Very occasionally the myocardial nuclei were found to be swollen and vacuolated (figure 2).

The right lung weighed 650 gm. and the left 450 gm. The lungs were light and floated in water. Upon section numerous bullous air pockets collapsed. The walls

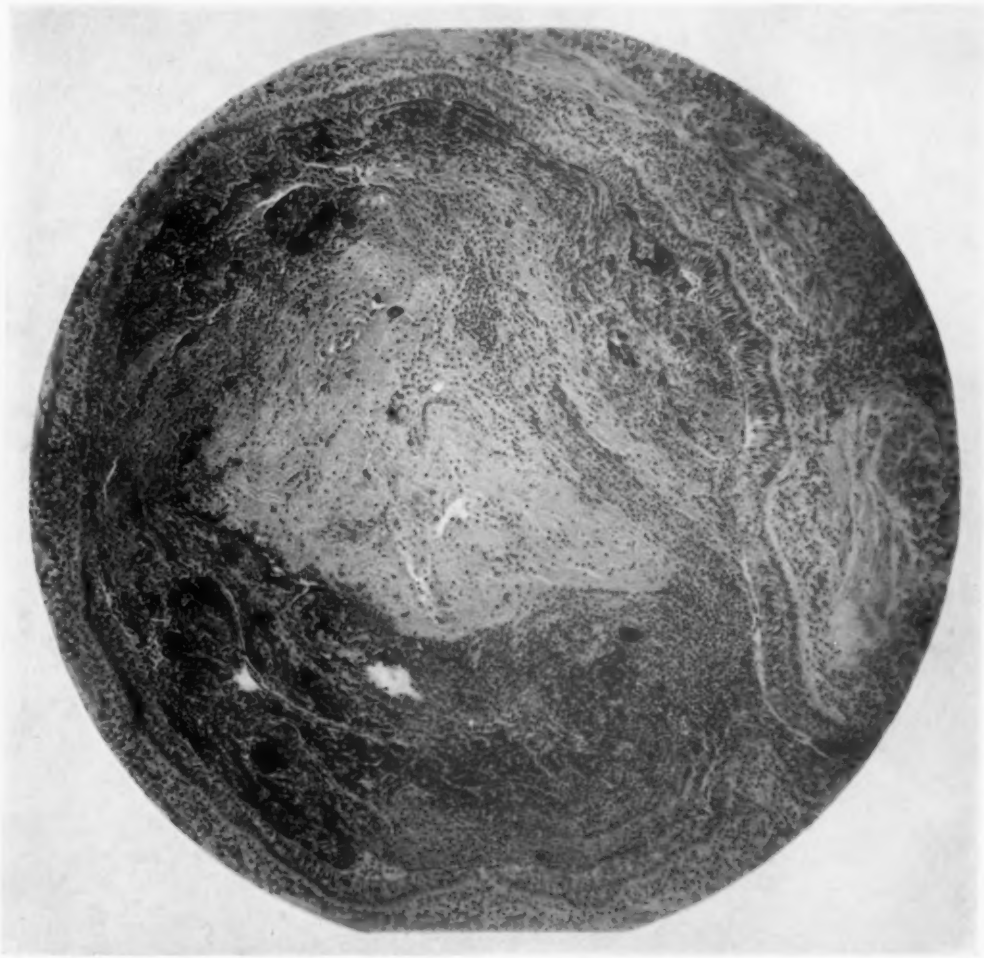

FIG. 4. Bronchiole containing mucopurulent plug in which are found numerous eosinophilic polymorphonuclear leukocytes.

of the terminal bronchioles were more prominent than usual and from their lumina mucinous plugs were expressed. Local areas of pneumonic consolidation were scattered throughout both organs. Mucinous material was found in the larger bronchi but did not occlude the lumina. Histologically, the alveolar spaces in some areas were few in number and of great size. Many of the intervening septa had broken. The walls were thin and their capillaries were collapsed (figure 5). Scattered throughout were patchy areas in which the alveoli were filled with inflammatory exudate consisting of neutrophilic leukocytes, many eosinophilic leukocytes, and fibrin. Adjacent to these areas were often seen strands of fibrin into which fibroblasts were

infiltrating in places completely replacing the exudate in the alveoli (figure 6). Lymph vessels were frequently plugged with a cellular exudate consisting almost entirely of eosinophilic leukocytes. Branches of the pulmonary artery had a thickened intima owing primarily to a proliferation of the fixed intimal cells together with a moderate infiltration of the interspaces by eosinophilic leukocytes. Occasionally thrombi were found in the smaller branches of the pulmonary arteries. The bronchial

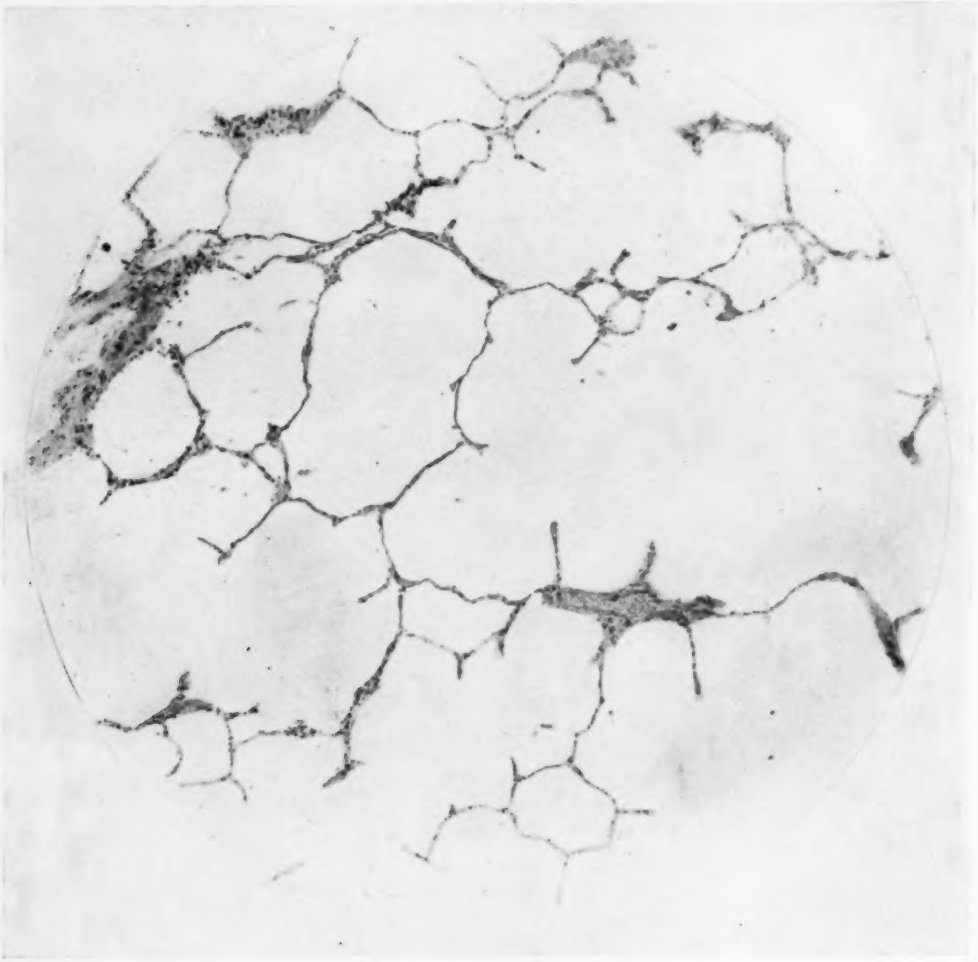

FIG. 5. Pulmonary emphysema.

mucosa was thrown into many folds, and the lumina were often filled with mucus with and without a cellular exudate (figure 4). The mucosal epithelium in many areas had undergone squamous metaplasia or was desquamated or consisted of low cuboidal epithelium. The basement membrane was well defined, in places hyalinized, and measured up to 32 micra in thickness. The bronchial glands were distended with abundant deep staining basophilic mucus resulting in obliteration of the cell outline and of the lumina of the glands. The smooth muscle of the bronchial tree was not appreciably thicker than that of controls (figure 3).

The marrow from the lumbar vertebra was red and granular, whereas that taken from the upper third of the humerus was red and soft in consistency. Microscopically, the quantitative relationship between hemopoietic and fatty tissue was within the average range. A differential count revealed that the eosinophilic myelocytes, metamyelocytes, and leukocytes were 22 per cent of the total nucleated cells in the bone marrow (figure 1).

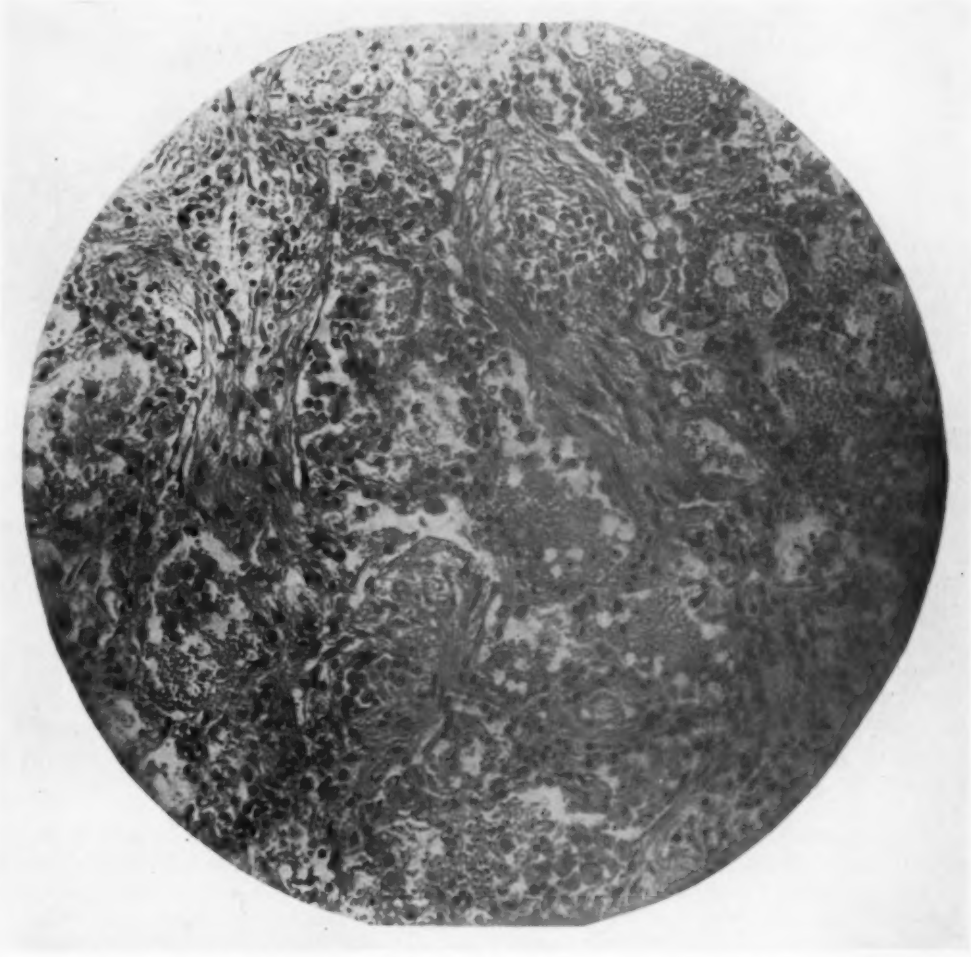

FIG. 6. Organizing pneumonia. Fibrous tissue may be seen growing into some of the alveolar spaces.

Pathological Diagnosis: Bronchial asthma (clinical), pulmonary emphysema, chronic bronchitis, bronchopneumonia, acute diffuse myocarditis with marked infiltration by eosinophilic leukocytes, eosinophilia of the bone marrow, cardiac hypertrophy and dilatation of right ventricle, and obesity.

Case 2. W. K., white male, aged 38, was admitted March 3, 1934.

History: The patient first noted frequent nasal and sinus inflammation about 10 years before death. These gradually took the form of asthmatic attacks with fre-

quent exacerbations of symptoms which gradually became worse and refractory to treatment. Frequent trips into warm dry climates were without benefit. There were three of four siblings with hay fever or asthma.

Physical Examination: On the day of admission the temperature was 98 to 99° F., pulse 110 to 130, respirations 20 to 35, and the blood pressure 120 mm. Hg systolic and 80 mm. diastolic. The patient was a poorly developed, greatly emaciated male in severe asthma. All teeth had been removed. The heart sounds were not remarkable. The chest findings were typical of asthma.

Laboratory Findings: The white blood count was 12,500. The differential count showed neutrophilic leukocytes 76 per cent, lymphocytes 24 per cent, eosinophilic leukocytes 0 per cent.

Course: The patient was given adrenalin, oxygen, and morphine with little effect upon his asthma. Sudden death occurred on the fourth hospital day.

Postmortem Examination: The heart weighed 330 gm., and the myocardium was red and coarsely striated. The right ventricle was 3 to 4 mm. in thickness, and the left 11 mm. There was moderate atherosclerosis of the coronary arteries. There was some fibrosis of the myocardium in the region of the papillary muscles. Microscopically, infiltration by inflammatory cells was observed. The coronary arteries showed slight intimal thickening.

The right lung weighed 660 gm., and the left 350 gm. The organs were voluminous, pale gray in color; crepitation was marked; and there were some bullous-like sacculations scattered over the surface. The bronchi were dilated but not sacculated, and contained a semi-thick yellowish-gray mucoid material. Several sections microscopically showed dilated bronchi partially filled with mucopurulent debris containing a few eosinophilic leukocytes. There was slight thickening of the basement membrane, with peribronchial fibrosis and moderate lymphocytic and plasma cell infiltration, but no apparent variation in the size of the bronchial musculature. The openings of the mucous glands were fairly prominent, but the glands themselves contained only a slight amount of mucus. The pulmonary arterial branches were unusual in that the intima was thickened and showed a tendency toward rarefaction. The alveolar spaces in many areas were partially filled with neutrophilic leukocytes and large mononuclear cells. In other places the walls had been ruptured and the spaces were large and empty.

No bone marrow was available for study.

Pathological Diagnosis: Bronchial asthma (clinical), pulmonary emphysema, chronic bronchitis, sclerosis of the pulmonary arteries, bronchopneumonia, arteriosclerosis, and fibrous pleurisy.

Case 3. J. P., white male, aged 41, was admitted May 8, 1938.

History: The first admission was in June 1935 following an upper respiratory infection which had brought on an asthmatic attack. The first attack of asthma followed pneumonia in 1926. The second attack occurred in 1930 after a cold. There were 10 admissions to the hospital for relief of asthma in the intervening years. Bronchoscopic lavages gave temporary relief. Lipiodol studies revealed considerable bronchiectasis. The final admission was after five days of status asthmaticus.

Physical Examination: The temperature was 98 to 104.5° F., pulse 70 to 170, respirations 45 to 60, blood pressure 138 mm. Hg systolic and 80 mm. diastolic. The patient was typical of one seen in status asthmaticus, many rhonchi and coarse râles being audible over both lung fields.

Laboratory Findings: The white blood count was 20,500. The differential count showed neutrophilic leukocytes 86 per cent, lymphocytes 14 per cent, and eosinophilic leukocytes 0 per cent.

Course: Adrenalin, asthmolysin, and morphine were given without relief. Nasal oxygen was administered. The patient died on the second hospital day, having had no relief from his asthma.

Postmortem Examination: The heart weighed 270 gm. The right ventricular wall averaged 7 mm. in thickness, and the left 14 mm. The right ventricle was dilated. Grossly the organ was otherwise normal. Microscopically, there were no significant changes. There was no inflammatory reaction, and the vessel walls were thin.

Lungs: The right lung weighed 630 gm. and the left 660 gm. The pleura was covered by dense fibrous adhesions. Numerous emphysematous blebs were present in the apex and anterior margins of the right lung. The lung was abnormally firm and darkly pigmented. The left lower lobe was markedly hyperemic and edematous. The bronchi passing to the posterior portions of the lower lobes measured 2 to 2.5 cm. in diameter, and those passing to the anterior portions measured up to 1 cm. The cut surface of the lower lobes revealed bronchopneumonia. The upper lobes showed areas of emphysema. The bronchi were filled with a tenacious mucopurulent material. The intima of the pulmonary arteries revealed numerous atheromatous plaques ranging from 2 to 5 mm. across. Many sections microscopically showed bronchopneumonia. One of the larger bronchioles showed a hyalinized thickening of the basement membrane which measured up to 30 micra in places. The epithelium was partially desquamated. The smooth muscle was somewhat hypertrophied in comparison with the control specimens. The mucous glands were numerous, and their lumina were distended with a mucopurulent exudate. There was massive infiltration of the tissues of the bronchi and interstitial tissue of the lung by lymphocytes, plasma cells, and moderate numbers of eosinophilic leukocytes. There was some peribronchial increase in fibrous tissue. The lumina of the bronchi contained varying quantities of mucopurulent material. The medium and large sized arteries showed marked intimal thickening and atheromatous rarefactions, and their walls were infiltrated by a few lymphocytes and plasma cells.

The bone marrow from the lumbar vertebra and sternal body was red and hyperplastic. Marrow from the upper third of the humerus was red at the periphery and fatty centrally. Bone marrow differential count revealed 1.7 per cent eosinophilic myelocytes, metamyelocytes, and leukocytes. The other constituents of the marrow fell within the normal range.

Pathological Diagnosis: Bronchial asthma (clinical), chronic bronchitis, pulmonary emphysema, bronchiectasis, chronic pneumonitis, bronchopneumonia, hypertrophy and dilatation of the right ventricle, arteriosclerosis of the pulmonary arteries.

Case 4. J. G., white male, aged 70, was admitted March 5, 1934.

History: Three years after an attack of pneumonia at the age of 15 the patient had his first asthmatic attack. Since then, with the exception of a 10 year period, he had had perennial asthma occurring in unseasonable weather and as often as once a week. For two or three years preceding death he suffered from "smothering attacks," not accompanied by pain, which were so severe as to cause him to jump out of bed. Increasing edema of the extremities was described.

Physical Examination: The temperature was 98 to 101° F., pulse 100, respirations 20 to 50. The patient was markedly cyanotic, dyspneic, and emaciated. The chest was barrel-shaped, with poor expansion. The heart sounds were normal. There was dullness at the right base, with wheezing respirations. Marked pitting edema of the lower extremities and the back was found.

Laboratory Findings: White blood count was 13,000. No differential count was recorded.

Course: Venesection on two occasions and nasal oxygen did not stop an unfavorable course with death on the third hospital day.

Postmortem Examination: The heart weighed 400 gm. The left ventricle measured 18 mm. in thickness and the right 16 mm. The right auricle and ventricle appeared dilated. There was some thickening along the line of contact of the leaflets of

the mitral and tricuspid valves and of the cusps of the aortic valve. There were some arteriosclerotic plaques of the intima and narrowing of the lumina of the coronary arteries. Histologically, there was intimal thickening of the coronary arteries, but there was no inflammatory change in the myocardium.

The right lung weighed 720 gm., the left 800 gm. The visceral pleura was 2 to 3 mm. thick. There was hypostatic congestion. The bronchi appeared dilated, and there was an increase in parenchymatous fibrous tissue. Microscopically, some bronchioles contained cellular and basophilic debris and an occasional neutrophilic leukocyte. There was metaplasia of the lining epithelium of the bronchioles in places. Some of the alveoli contained red blood cells, large mononuclear cells, and occasional neutrophilic leukocytes. Numerous emphysematous areas were found. The mucous glands were distended with mucus, but the basement membrane was not thickened. The smooth muscle was apparently not hypertrophied. Numerous lymphocytes, plasma cells, and occasional neutrophilic leukocytes were infiltrated in the surrounding fibrous tissue. No eosinophilic leukocytes were seen. One or two arterioles showed hyalinization of their walls with atheromatous spaces in the intima.

No bone marrow study was made.

Pathological Diagnosis: Bronchial asthma (clinical), emphysema, cardiac hypertrophy (right ventricle), anasarca, fibrous pleurisy, fibrosis of the lung apices, chronic passive hyperemia of internal organs.

Case 5. C. C., white male, aged 34, was admitted August 31, 1938.

History: There was a history of asthma since childhood. One week before admission he complained of malaise. There was no definite chill, but progressively severe cough producing rusty sputum was noted.

Physical Examination: The temperature was 100 to 104.5° F., pulse 120 to 160, respirations 40 to 55, and blood pressure 118 mm. Hg systolic and 70 mm. diastolic. There was dyspnea and cyanosis. The entire chest was filled with coarse râles, and a friction rub at both bases was heard. Heart sounds were indiscernible.

Laboratory Findings: The white blood count was 18,500. The differential count showed neutrophilic leukocytes 95 per cent, lymphocytes 5 per cent, and eosinophilic leukocytes 0 per cent.

Course: In spite of oxygen and other supportive measures the patient grew steadily worse and died on the third hospital day.

Postmortem Examination: The chest was barrel-shaped, the anterior-posterior diameter being greater than the transverse diameter.

The heart weighed 400 gm. The left ventricle averaged 20 mm. in thickness, the right 7 mm. The trabeculae carneae and papillary muscles were definitely thickened on the right. The intima of the coronary arteries was thin and smooth except for an occasional yellow plaque. Histologically, near the endocardial surface there was mild myocardial fibrosis. There were collections of lymphocytes, plasma cells, and a few neutrophilic leukocytes in some of the intermuscular spaces. No eosinophilic leukocytes were seen. The fibers seemed increased in size, with evidence of degeneration in places.

The right lung weighed 1130 gm., and the left 1120 gm. The anterior two-thirds of the right and left lower lobes and the entire right and left upper lobes were large, firm, and non-crepitant. The cut surface was red, gray, and moist, and the bronchi were filled with reddish pink frothy material. Histologically, the vessels were congested, and the alveolar spaces were partially obliterated by neutrophilic leukocytes and large mononuclear cells. There was no significant increase in fibrous tissue, but one small bronchiole was seen and its mucosa was considerably desquamated. The walls were not noticeably thickened and the basement membrane could not be delineated. No bronchial glands were included in the one section available for study.

Bone marrow from the lumbar vertebra and the upper third of the humerus was red. The differential count revealed the eosinophilic myelocytes, metamyelocytes, and

leukocytes to be 2.2 per cent of all nucleated marrow cells. The remainder of the elements were within the average range.

Pathological Diagnosis: Bronchial asthma (clinical), bronchopneumonia, serofibrinous pleurisy, acute non-suppurative myocarditis, and hypertrophy of the right ventricle.

Case 6. F. M., white male, aged 60, was admitted June 15, 1939.

History: The first admission was in 1933 with a history of asthma for the preceding 10 to 15 years. Frequent attacks had occurred but were without serious effect until four days prior to his final admission when he noted pain in the left chest which remained throughout most of the night. This was accompanied by wheezing and fever. He had had a sinusitis in the past. Dependent edema had been present for the preceding four years.

Physical Examination: On admission the temperature was 103° F., pulse 120, respirations 24, and blood pressure 140 mm. Hg systolic and 84 mm. diastolic. There was a paroxysmal cough occurring about every 15 minutes during the examination. There was moderate dyspnea, and the expiratory phase of respiration was emphasized. There were many moist râles and rhonchi over the lungs. Heart sounds were not remarkable. Varicosities and pitting edema were observed in both legs.

Laboratory Findings: The white blood count was 21,000. Differential count showed the neutrophilic leukocytes to be 80 per cent. No eosinophilic leukocytes were recorded.

Course: Three days after admission the patient developed a sudden rise in temperature to 105° F., pulse to 145, and respirations to 40. Bronchoscopy and aspiration of heavy mucopurulent secretion from the trachea and right bronchus resulted in dramatic relief of symptoms. Two days later he became irrational, developed signs of pneumonia over the right base, and died on the eighth hospital day with a temperature of 106° F.

Postmortem Examination: The heart weighed 410 gm. The left ventricle averaged 16 mm. in thickness and the right 5 mm. There was moderate arteriosclerosis of the coronary arteries. The papillary muscles were hypertrophied. There was fusion at the commissure of the left and right coronary cusps of the aortic valve and associated with this there was calcification at the bases of these cusps. Histologically, the myocardial fibers were uniform in size and were not enlarged. No inflammatory reaction was seen.

The right lung weighed 1200 gm., and the left 700 gm. They were airless and of rubbery consistency. The bronchi showed areas of dilatation. Histologically, many sections showed hemorrhage into the alveoli and many patches of bronchopneumonia. There were areas of emphysema. Several of the larger bronchioles showed nearly complete mucosal desquamation with thickening and hyalinization of the basement membrane but no mucous plugs. There were numerous lymphocytes, plasma cells, and some eosinophilic leukocytes in the mucosa. The smooth muscle, although fairly prominent, showed no apparent variation from the controls. The bronchial glands showed moderate distention with basophilic staining material which partially obliterated the cellular outline. There was interstitial fibrosis of the lung with lymphocytic and plasma cell infiltration.

The marrow from the lumbar vertebra and the upper third of the humerus was red. Histologically, the cell constituents fell within the normal range, since the differential count of the nucleated cells revealed the eosinophilic myelocytes, metamyelocytes, and leukocytes to be 1.4 per cent of the total.

Pathological Diagnosis: Bronchial asthma (clinical), pulmonary emphysema, chronic interstitial pneumonitis, bronchopneumonia, chronic bronchitis, and generalized arteriosclerosis.

TABLE I

HISTOLOGICAL FINDINGS	I	II	III	IV	V	VI
Pulmonary emphysema	Moderate	Marked	Marked	Present; moderate	Slight (1 section)	Present
Chronic pneumonitis	Extensive organized pneumonitis	None	Interstitial pneumonitis. Organizing pneumonia	None	Insufficient data (1 section)	Interstitial pneumonitis. Organizing pneumonia—early
Chronic bronchitis	Extensive	Present	Present	Present	Insufficient data	Present
Pulmonary arteriosclerosis	Slight	Moderate	Marked	Slight	Insufficient data	None
Acute bronchopneumonia	Extensive	Present	Present	Present	Present	Present
Pulmonary endarteritis (active)	Present	None	None	None	Insufficient data	None
Thickening of basement membrane	Thickened	Slight	Thickened	None	Insufficient data	Thickened
Hypertrophy of bronchial musculature	?	None	?	None	Insufficient data	Normal
Mucinous plugs in small bronchi	Present	Moderate number of bronchi filled with mucus	Present	None	Insufficient data	None
Eosinophilic infiltration of peribronchial tissues	Marked	None	Slight	None	None	Moderate
Sacculation of bronchi	Dilated only	Dilated only	Dilated only	Slight	—	Marked
Distention of bronchial glands and ducts with mucus	Bronchial glands distended with mucus	Essentially normal	Bronchial glands distended with mucus	No bronchial glands in sections	Insufficient data	None
Myocarditis	Acute diffuse myocarditis with infiltration by large numbers of eosinophiles	None	None	None	Non-suppurative myocarditis	None
Eosinophilic, myelocytes, metamyelocytes and leukocytes in bone marrow	22%	—	1.7%	—	2.2%	1.4%
Eosinophilia in blood	14%	0	0	Not done	0	0

Discussion

The essential findings in each case are tabulated in table 1. The last two cases are included as asthmatics who died from pneumonia; the fourth died in cardiac failure. As already noted, the material for study in Case 5 is limited, but it was included because of the cardiac findings. Excluding that case for a moment, we note that pulmonary emphysema, chronic bronchitis, and bronchopneumonia were present in each case, and pulmonary arteriosclerosis in all but the last. Cor pulmonale was present in two. In one (Case 1) the well developed right ventricular hypertrophy was secondary to the chronic pneumonitis, and in the other (Case 4) a longstanding emphysema accounted for the enlargement. Thickening of the basement membrane was present in all but the fourth case. Mucous plugs in the small bronchi were present in two instances, distention of the glands with mucus in three, eosinophilic leukocytic infiltration of the peribronchial tissues in four, and dilatation of the bronchioles in four. Pulmonary endarteritis was noted in but one case. Hypertrophy of the bronchial musculature has often been cited as one of the necessary criteria in making the pathological diagnosis of asthma.[1, 3, 4, 5] We compared our microscopic sections with those obtained from patients who had died from other than pulmonary diseases. It was our impression that, in our series, there was no appreciable variation in the size of the smooth muscle bundles. At the same time we measured the thickness of the basement membrane in the controls and found it nowhere to be more than 16 micra, a figure which was exceeded in our series as noted above.

For the past three years the Pathology Service has been doing routine bone marrow studies on all cases. In order to obtain an accurate evaluation on the four cases in our series, one of us (J. R. R.) counted not less than 1000 nucleated cells in each instance. Two counts of 500 cells each that checked were accepted. For controls similar counts were made from 10 normal cases. These slides were obtained from patients who had died a traumatic death and who exhibited no pathologic change other than that incurred by the accident. The counts of eosinophilic cells obtained from this normal group were found to range between a maximum of 3.96 per cent and a minimum of 0.6 per cent with a mean value of 2.26 per cent. Comparing these figures with those noted in the series it is interesting to find that three of the four cases studied have values that fall well within the normal range. It is regretted that only two of these four cases died a truly asthmatic death, but the findings in these two cases in the light of the control group are significant. In one instance (Case 3) a count of 1.7 per cent was obtained, and in the other (Case 1) the count was 22 per cent (figure 1). This patient was the only one in which an eosinophilia (14 per cent) was recorded in the peripheral blood stream. Nothing was found in the literature to explain the amazingly high eosinophilia found in the marrow. It certainly is not a consistent finding in asthmatic fatalities, as we have shown. On the other

hand, it may be present in cases in which there is a peripheral eosinophilia from any cause. One must withhold any conclusions until further bone marrow studies have been performed and merely state that this finding of an eosinophilia in the bone marrow of asthmatic patients is unusual.

In Case 1, along with an eosinophilia in the bone marrow, there was noted an infiltration of numerous eosinophilic leukocytes into the myocardium and lungs as part of the inflammatory reaction in these organs. The pathological picture could not be duplicated in asthmatic cases in the literature. Karsner, in his textbook,[6] discusses a type of myocarditis following pneumonia and other infectious diseases. The description does not correspond with the findings in our case. Boyd[7] describes an acute parenchymatous myocarditis following such toxic conditions as diphtheria. Although he notes that if death occurs early in the disease there is no inflammatory change, he does not detail the findings seen by us. In one report[8] two cases of syphilis were described in which there was an eosinophilic leukocytic infiltration of the myocardium following treatment with salvarsan and bismuth. Although the author found areas of necrosis in the muscle somewhat similar to our findings, yet the lesions themselves contained giant cells, and were described as being tuberculoid in appearance. He favored the view that this eosinophilic myocarditis was allergic in origin. One case in our series, in which there was found a non-suppurative myocarditis, had a long asthmatic history and hence is of value for comparative purposes. In this case (Case 5) the cellular response of lymphocytes, plasma cells, and large mononuclear cells, although typical of that described by the textbooks, is entirely different from that seen in our first case (figure 2) in which the eosinophilic leukocytes are not only the predominating cell in the necrotic areas, but also are found in large numbers elsewhere in the myocardium.

It is possible again to conjecture that this reaction is concomitant with a general peripheral eosinophilia. It also may be present during an attack of asthma in which the blood eosinophilic count is elevated, only to disappear along with some of the other pathologic findings as was suggested by Thieme and Sheldon.[4] Further study will have to be done to clarify this issue. Certainly at the present time it appears to be a very rare condition.

Summary

Six cases of bronchial asthma with autopsy findings are presented. Three of these died in status asthmaticus. The majority of the anatomical lesions described in asthma were present. Bone marrow studies are described in four cases. In one case which had a large preponderance of eosinophilic myelocytes, metamyelocytes, and leukocytes in the bone marrow, there was also found an acute diffuse myocarditis with tremendous infiltration of eosinophilic leukocytes. A review of the literature has not revealed any report of similar bone marrow or myocardial findings in fatal asthma.

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FAT EXCRETION IN THE BOWEL OF MAN *

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In general it has been thought that the fat and fatty acids found in feces represent unabsorbed fat of food. In recent years, some changes in this point of view have occurred. Hill and Bloor,[1] in 1922, found that certain portions of the fat in the feces of dogs were of the type excreted by the intestinal tract. In 1924, Sperry and Bloor [2] demonstrated that fat appeared in the feces of cats and dogs on a fat-free diet. This was confirmed by Holmes and Kerr,[3] in 1923. Sperry [4] and Sperry and Angevine [5] concluded that desquamation of intestinal epithelium was not an important source of these lipids and that when dogs received a lipid-free diet the amount of lipids excreted from ileac fistulas was much greater than the amount excreted in the feces. Previously, Beumer and Hepner [5] and Bürger and Oeter [5] found that the amount of cholesterol in the intestinal contents was greater in the colon than it was in the ileum of dogs and cadavers. In 1934, Krakower,[6] who studied 20 normal persons, assumed that when fat was given in moderate amounts the fecal lipids did not represent a residue of unabsorbed fat but probably represented an excretion of the lipids of the blood into the intestinal tract. Finally, as a result of study of a patient who had a fistula of the ileum, Doubilet and Reiner [7] concluded that the ileum secreted a fluid which contained about 2 per cent of lipids.

Method and Results of Observation

In order to obtain more information about the excretion of fat by the intestine of man, observations were made on 14 human beings. Subject 1 had undergone an ileocolostomy and resection of the right portion of the colon and subject 2 had undergone an ileocolostomy. The observations on subjects 1 and 2 were made about 20 days after the respective operations had been performed. Subject 3 had undergone an ileostomy and subsequent resection of the right half of the colon and approximately four inches of the terminal portion of the ileum. Subjects 4, 5, 6, 7 and 8 had thrombo-ulcerative colitis which involved the entire colon. Subjects 9 and 10 were normal persons who received a fat-free diet. Subjects 11, 12, 13 and 14 had thrombo-ulcerative colitis.

Subject 1 received a fat-free diet for 10 hours; all food was withheld for 14 hours before the diet was given and for 14 hours after the diet was discontinued. Subjects 2 and 3 received a fat-free diet for 36 hours; but all

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food was withheld for 12 hours before the diet was administered. In the observations made on subjects 4, 5, 6, 7 and 8 the dietary regimen was the same as that used for subject 1. Subjects 9 and 10 received a fat-free diet for 84 hours. Subjects 11, 12, 13 and 14 received a high-fat diet. Previous analyses had disclosed that the intestinal excretion of fat by these four subjects was within normal limits when a regular diet was administered. The observations on subjects 11, 12, 13 and 14 were made to determine the effect of a high-fat diet on the intestinal excretion of fat by patients who have thrombo-ulcerative colitis. This was done for the purpose of determining the excretion of fat in cases in which a high-fat diet was received.

The fat-free diet was made up of vegetables and fruits, sugar, jelly and candy. It furnished approximately 2000 calories in 24 hours (table 1) and contained approximately 1.65 gm. of fat.

Carmine was administered one hour before the first meal and immediately after the last meal of the fat-free diet. Charcoal was given with the first meal after the fat-free diet had been discontinued. After the administration of the first dose of carmine, each stool that contained the dye was collected in a special box marked with the date and time of passage. Some of these were examined separately; some were collected, mixed and analyzed as one specimen, as the data obtained from single stools and mixtures of the stools of any given subject were entirely comparable. Care was taken to avoid contamination with urine. Gauze was used to receive the excreta of subject 3, from the ileac stoma. In all observations the collection of feces and ileac discharges was continued until the appearance of the charcoal, and each stool passed was inspected for carmine and charcoal. The specimens were preserved in the refrigerator when they could not be examined immediately.

The amount of total fat in the feces was determined by the Fowweather [8] modification of Saxon's method. All results were calculated in terms of percentage of the dry feces.

The observations on subjects 11, 12, 13 and 14 were made while the subjects were receiving a high-fat diet. Two observations were made on subject 11; the first, while the patient had generalized edema. During each observation the patient received 120 gm. of fat daily. The stools that were passed during each observation were mixed and were examined as a single specimen. The value for the total fat in the mixed specimen of the stools that were passed during the first observation was 29.7 per cent of the dry matter. The second observation on subject 11 was made after the edema had decreased and disclosed 21 per cent of dry matter, 13.8 per cent of which consisted of fat.

Subject 12 received approximately 185 gm. of fat daily; 9.5 per cent of the dry matter in the mixed specimen of stools consisted of fat.

Subject 13 received 200 gm. of fat daily. A mixed specimen of the stools contained 12 per cent of dry matter, 10.2 per cent of which consisted of fat.

TABLE I

Intestinal Excretion of Fat (14 Cases)

Subject		Conditions of Experiment	Dry Matter, Per cent of Stools Examined	Total Fat,* Per cent	Fat, Gm.	Neutral Fat,* %	Fatty Acids,* %	Soap*
No.	Condition							
1	Ileocolostomy and resection of right half of colon	Fasted 14 hours; fat-free diet 10 hours and then fasted 14 hours	18.6	1.24	2.76	0.104	1.136	
2	Ileocolostomy	Fasted 12 hours; fat-free diet 36 hours	Second stool, 7.2 Third stool, 6.8 Fourth stool, 6.4 Fifth stool, 20.8	Second stool, 0.72 Third stool, 0.4 Fourth stool, 0.44 Fifth stool, 1.48	3.76	0.12	1.4	
3	Ileostomy and resection of right half of colon and terminal portion of ileum	Fasted 12 hours; fat-free diet 36 hours	First spec., 6.3 Second spec., 6.3	First spec., 0.4 Second spec., 0.36	5.75	0.25	0.11	
4	Thrombo-ulcerative colitis	Fasted 12 hours; fat-free diet 36 hours	Second, third, fourth and fifth stools, 6.0	1.0	4.8			
5	Thrombo-ulcerative colitis	Fasted 12 hours; fat-free diet 36 hours	Second, third, fourth stools, 7.6 Fifth and sixth stools, 8.0	0.40 0.6	4.6	0.133 0.177	0.227 0.223	0.04 0.20
6	Thrombo-ulcerative colitis	Fasted 12 hours; fat-free diet 36 hours	Four stools, 5.0	0.96	3.84	0.354	0.223	0.38
7	Thrombo-ulcerative colitis	Fasted 12 hours; fat-free diet 36 hours	All stools mixed	1.08	4.0	0.398	0.272	0.41
8	Thrombo-ulcerative colitis	Fasted 12 hours; fat-free diet 36 hours	Second, third, fourth stools, 9.18 Fifth, sixth and seventh stools, 9.0	0.6 0.4	4.5	0.34	0.26	
9	Normal person	Fasted 12 hours; fat-free diet 36 hours	First stool, 21.24 Second stool, 29.24	1.4 1.34	14.0	0.31 0.66	1.43 0.62	0.66 0.06
10	Normal person	Fasted 12 hours; fat-free diet 36 hours	First stool, 18.4 Second stool, 32.0	1.20 0.94	10.7	0.45 0.14	0.51 0.66	0.24 0.14
11	Thrombo-ulcerative colitis	Fasted 12 hours; 120 gm. fat given daily. Patient had edema, 3+	Stools mixed during edema. After edema decreased, 21.0	29.7 13.8	70.5			
12	Thrombo-ulcerative colitis	Fasted 12 hours; 185 gm. fat given daily	Stools mixed	9.5	38			
13	Thrombo-ulcerative colitis	Fasted 12 hours; 200 gm. fat given daily	Stools, 12	10.2	24.4			
14	Thrombo-ulcerative colitis	Fasted 12 hours; 120 gm. fat given daily	Stools mixed	3.24	12.7			

* Expressed in percentage of dry matter.

In observing subject 14, who received a high-fat diet, the stools were mixed and were examined as a single specimen; 3.24 per cent of the dry matter in this specimen consisted of fat.

Comment

The number of observations reported is small, but we believe that the results are of value in confirming those obtained on animals and that they indicate a significant variation in the excretion of fat under different circumstances. Excretion of fat by normal persons was greater than excretion of fat by patients who had been subjected to resection of the right portion of the colon. Furthermore, excretion of fat by patients who had thrombo-ulcerative colitis was less than excretion of fat by normal persons, but was greater than excretion of fat by the patients who had been subjected to resection of the right half of the colon.

It is true that the amount of fat in the feces of the subjects who received a fat-free diet varied, but an average of 0.79 per cent of total fat was excreted by persons who had been subjected to an ileostomy or an ileocolostomy; an average of 0.81 per cent was excreted by persons who had thrombo-ulcerative colitis; and an average of 1.23 per cent was excreted by normal persons; however, the deviation from the averages is considerable. These facts would suggest that the large intestine itself plays a part in the excretion of fat and that the greatest excretion occurs in the proximal segments of the large intestine. The entire intestinal wall is injured in cases of thrombo-ulcerative colitis. It has been pointed out previously by Curry and Bargen [9] and by Whittaker and Bargen [10] that the colon serves both as a secretory and excretory organ.

Verzár and McDougall [11] expressed the opinion that absorption of fat does not take place in the cecum. They said that "practically all the fat ingested is absorbed by the time chyme enters the large intestine, and no fat whatever seems to be absorbed there." Welch, Adams, and Wakefield [12] did not find any change in the absorption of fat in cases of thrombo-ulcerative colitis and they suggested that fat is not absorbed in the colon. Satisfactory proof that absorption of fat occurs in the cecum does not exist. However, the suggestion that excretion of fat occurs in the cecum and ascending colon seems clear.

It is noteworthy that in cases in which the amounts of neutral fat, fatty acids and soap were determined, the excretion of fatty acids was greater than that of neutral fat. This may be the result of normal digestive processes or the result of an unexplained activity of the mucosa. In this connection it may be well to remember that Brown, Hansen, McQuarrie and Burr [13] pointed out that in one case the concentration of fatty acids in the serum was lower when the intake of fat was 2 gm. per day for a period of more than six months than it was when the patient received a normal diet.

Conclusion

Excretion of fat by the intestine occurs when human beings receive a fat-free diet. This is suggestive of the possibility that the intestinal wall secretes fat. Our studies suggest that the large intestine excretes more fat than the small intestine. In cases of thrombo-ulcerative colitis the average excretion of fat is lower than the average excretion of fat by normal persons. This may be the result of injury of the intestinal wall.

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SOME NOTES ON CYSTIC DISEASE OF THE LUNGS, WITH A REPORT OF ONE CASE*

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It is our purpose to report a case involving the diagnosis of cystic disease of the lungs. Clinically, this case was diagnosed as congenital cystic disease of the lungs, but even with all the data before us, we wish to emphasize how difficult it is to make a definite differential diagnosis between congenital cystic disease of the lungs, acquired cystic disease of the lungs, and extensive

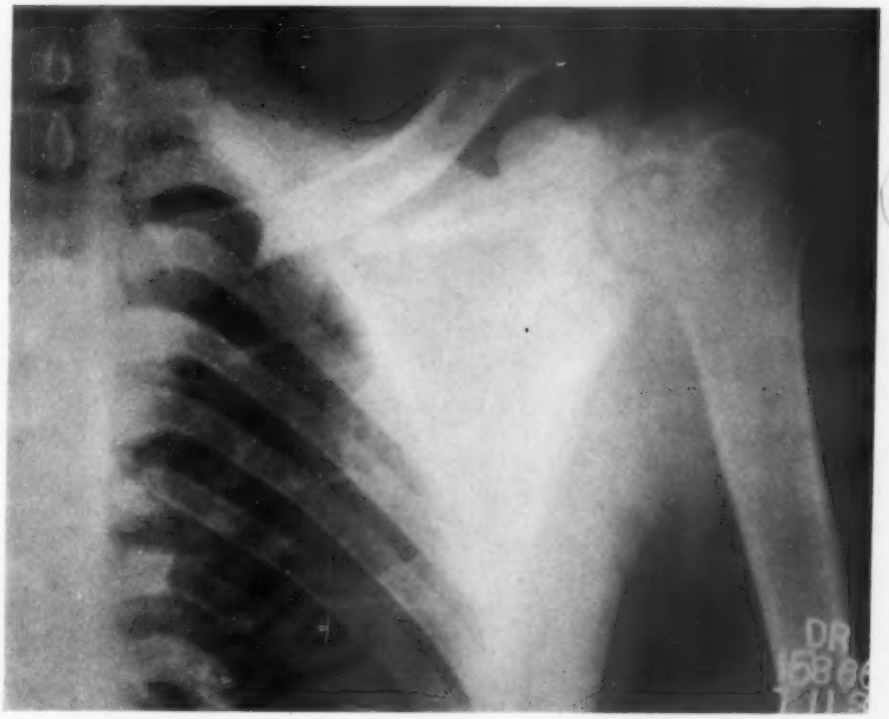

Fig. 1. 7-11-32. Reëxamination of the films of the shoulder made in 1932 showed some bullae which were overlooked in the first examination.

emphysema with bullous formation. The case is reported with its clinical and pathological findings. Roentgenograms of the lungs and also some actual photographs are shown.

In a case of multiple cyst-formation in the lung, the diagnosis might seem to be of academic interest only, because of the small likelihood that this type

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of case could be benefited by surgery. Since the literature of the subject, however, shows that some types of cystic disease of the lungs are amenable to surgical procedure, it is of definite importance to differentiate these conditions.

Case Report

C. J. I., aged 34, negro male, came in May 14, 1939, complaining of shortness of breath and indigestion. About four years previously he began to notice shortness of breath on exertion. His indigestion began about the same time. In late December

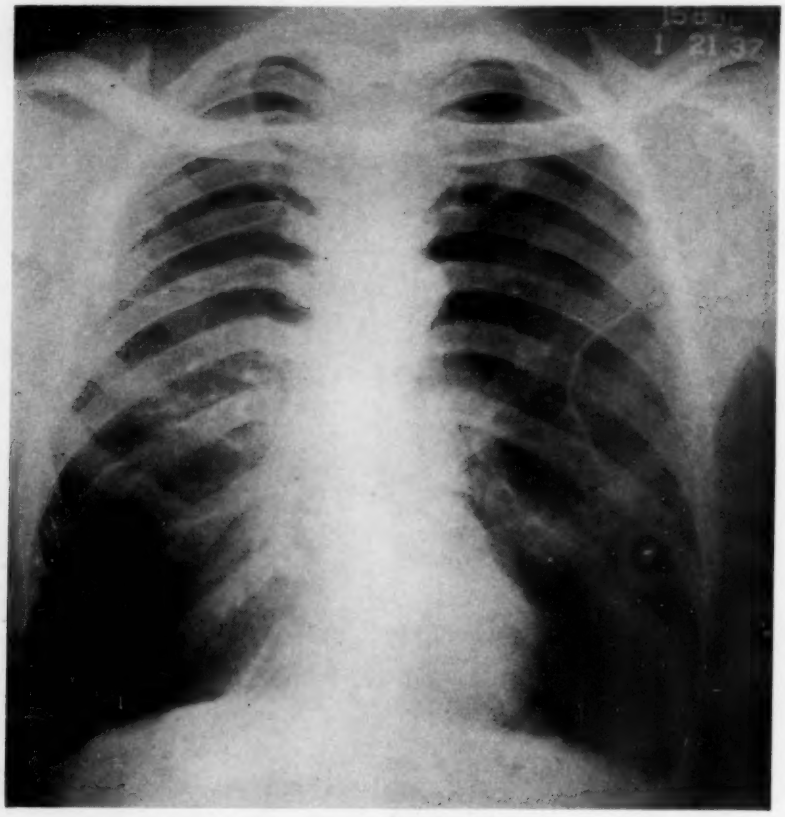

Fig. 2. 1-21-37. (A-P view.) The appearance is that of congenital cystic disease of the lung. The diaphragms are quite low and limited in mobility, and there are questionable small amounts of fluid at both costo-phrenic angles.

of 1937, he had an attack which his doctor diagnosed acute indigestion. He had been constipated for three days when he began to get pain in his abdomen and cardiac palpitation. He then became dizzy, began to perspire, and finally lost consciousness for a short time. He was very weak from this attack for several weeks. He continued to be short of breath and was conscious of palpitations and what he described as "heart flutter." He was sent to the hospital in November of 1938, and it was there found that he was quite anemic. He received two transfusions. About that time he noticed some swelling of the ankles. In February of 1939 he had influenza, and had become gradually more short of breath since that date until he was finally

not able to lie down in bed. He had a very annoying non-productive cough; if this occurred while he was lying down, he almost smothered. This caused him to be afraid to lie down. At times he sat up all night, being most comfortable when he leaned forward. During the preceding two years he had lost 40 pounds, for even small amounts of food caused gas, and this in turn produced dyspnea. He had no hemoptysis. He had some pain in the left chest in February, which the doctor diagnosed as pleurisy.

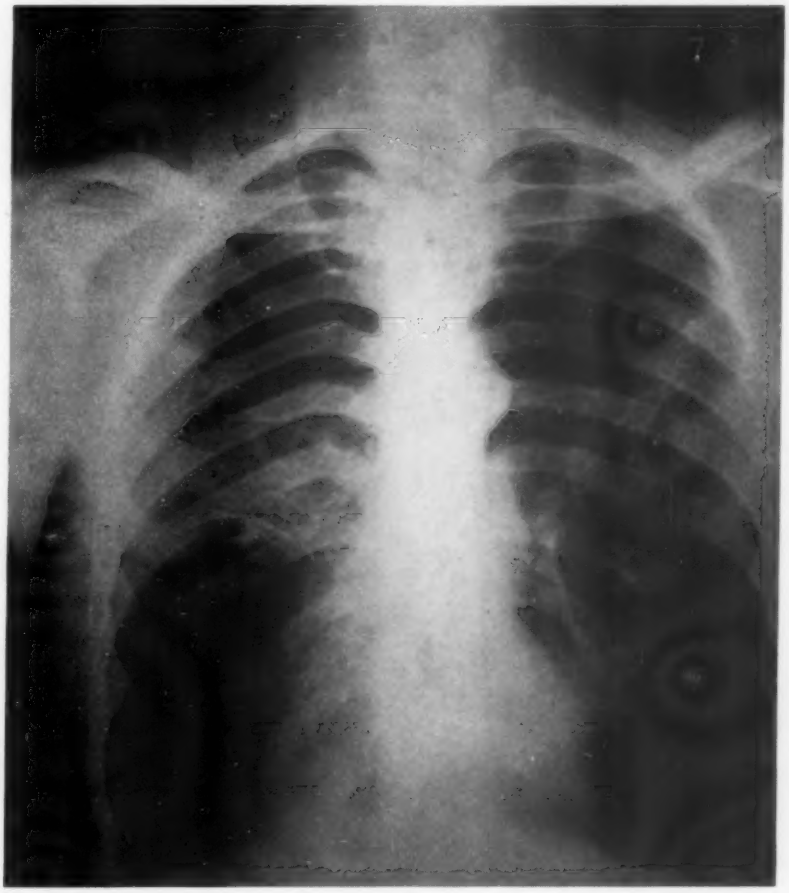

FIG. 3. (A–P view.) Reëxamination of the chest shows an increase in the extent of the process. There is only a small amount of lung tissue on the right, but slightly more on the left.

There were no night sweats. He had a slight wheezing at times. The rest of the history was practically negative, except that the patient stated that he had been quite athletic in college, being a long-distance runner and a football player. He further stated that he had had no dyspnea at that time. He drank heavily during 1937 and up until October of 1938. His family history was negative. His wife and three children were living and well.

Physical Examination. The patient had marked dyspnea which was increased by talking and also by movement of any kind. The head showed no gross abnormalities. The eyes were slightly prominent; the pupils were small but reacted to

light normally. Ocular movements were normal. The nose was unobstructed. Hearing was intact. Many of the posterior teeth had been removed. The gums showed some gingivitis. The tongue was moderately coated. The tonsils were back of red pillars. The neck showed some posterior cervical adenopathy. Veins of the neck were engorged. There was a three-inch operative scar over the outer end of the right clavicle, extending over the right shoulder. The chest showed expansion to be poor and equal. There was some retraction above and below both clavicles. There was some fullness of veins over the upper arms, more marked on the right. Little

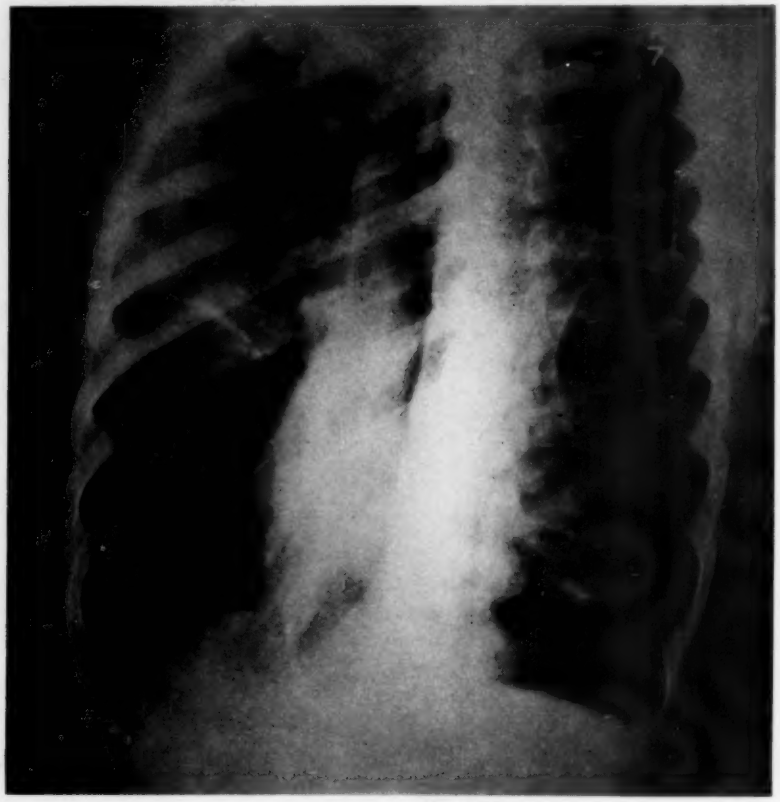

FIG. 4. 7–6–39. Oblique view.

if any movement of the diaphragm was made out. The percussion note over both upper lungs, front and back, was high pitched. It was more resonant over lower lungs, and seemed to be more resonant during inspiration. Breath sounds were markedly suppressed. Whispered voice was not increased. Tactile fremitus was present. The spoken voice seemed to be increased over both lungs. Examination of the heart showed the left border to be 7 cm. from the midline, and the right border to be 2.5 cm. from the midline. There was a diffuse cardiac impulse in the epigastrium. Blood pressure in the left arm was 114 mm. Hg systolic and 75 mm. diastolic, and in the right, 110 mm. systolic and 80 mm. diastolic. The rate was 108, and regular. There were no murmurs, and the sounds were of good quality, being heard best in the epigastrium. The abdomen was not remarkable except for a definite bulging of the upper right rectus muscle. There was marked tenderness in this region. There was a long

scar on the outer side of the left thigh resulting from operation for fascia graft on his right shoulder. The rectum, genitalia, and extremities were essentially negative.

He was admitted to Duke Hospital on July 3, 1939. The following is a report of the laboratory and roentgen-ray work done on admission:

The blood was within normal limits; urine was negative; sputum was negative for tubercle bacilli. The vital capacity of the lungs was 1.16 liters, 30.4 per cent

FIG. 5. The left lung.

normal. Roentgenogram of the chest showed "extensive areas of fibrosis throughout both lungs and in the left mid lung, there are definite annular areas, some of which are in the mid lung and others are possibly in the posterior pleura. Throughout the right lung, there are numerous fibrotic bands, or possibly small cystic areas, with collapse of small areas of lung. The diaphragms were quite low and limited in mobility and questionable small amounts of fluid in both costophrenic angles. This has the appearance of congenital cystic disease of the lungs, and is most unusual in its distribution." Electrocardiogram revealed right axis deviation and suggested myocardial damage. Wassermann and Kahn tests were negative.

Course in Hospital. On July 9, 1939, an attempt was made to do a diagnostic pneumothorax on the right chest. About 150 c.c. of air were injected. On the following day some lipiodol was injected, but unfortunately a spontaneous pneumothorax

FIG. 6. The right lung (cut surface).

developed on the right side, and the patient became much more dyspneic. The dyspnea was so marked that on the next day it was necessary to insert a trocar and apply continuous suction. This gave him some temporary relief, but his dyspnea gradually increased, and he died on July 14, 1939.

Autopsy Findings. The examination was limited to an abdominal incision. However, the heart and lungs were removed sub-diaphragmatically.

Gross Examination. Dr. Brodie C. Nalle, Jr.: The body was that of an emaciated 34-year-old colored male, weighing 124 pounds, and measuring 5 feet and

FIG. 7. The right lung.

11 inches in length. Ribs and other skeletal parts were quite prominent. There was an old healed scar over the right shoulder (acromio-clavicular approach). Otherwise, the external examination was negative.

The abdominal cavity was free from fluid and gas. All peritoneal surfaces were smooth and glistening and every organ appeared grossly normal.

The thoracic cage was entered through the peritoneal surface of the diaphragm. Neither pleural nor pericardial cavities contained any excess fluid. The right lower lobe showed a fibrinopurulent exudate over the base, and, in addition, the basal and parietal surfaces of the lobe were attached to the right dome of the diaphragm and to the lateral chest wall, respectively, by thin fibrous adhesions. The left lung was free of exudate and adhesions.

The right lung weighed 500 grams and the left, 450 grams. On the surfaces of both lungs were multiple emphysematous blebs of variable size and shape, the largest measuring 7 cm. in diameter, and the smallest, 7 to 8 mm. These cyst-like sacs covered the lung periphery in grape-like clusters and were formed by a thin, translucent, pleura-like membrane which contained dilated blood vessels. A probe introduced through a bronchus into several sacs failed to collapse them even though they appeared to be air-containing cysts.

The main bronchi were patent, and the bronchial nodes were not remarkable. Sectioning revealed many of the blebs to be of peripheral distribution. These cyst-like structures were present both on the periphery of the lung and also in the lung substance proper. Some were very near the hilus of the lung. The small amount of lung tissue remaining appeared to be free from consolidation and congestion.

Other organs were essentially negative.

Microscopic Examination. The significant findings in this case were limited entirely to the lungs. Routine sections (stained with hematoxylin and eosin) revealed marked areas of emphysema and atelectasis throughout the lung. Often large cystic areas surrounded by interstitial tissue were seen. Bronchial epithelium could not be demonstrated as a lining for any of these cysts. Much anthracosis was present which was seemingly engulfed by large mononuclears. Iron stain strengthened the opinion that the pigmented areas were anthracotic. It was thought that the emphysematous blebs might have been caused by a lack of elastic tissue. Elastic tissue stains showed an adequate amount of elastic tissue which had been ruptured in the emphysematous areas.

Bacterial stain of the pleural exudate showed clumps of Gram-positive cocci and singular Gram-positive diplococci. The lung tissue itself was free from bacteria.

Interpretation. We have no explanation for this condition in the lungs. There was no history of asthma nor was there any demonstrable bronchitis or other cause which might have produced partial obstruction of the bronchi. Whether this condition started as congenital cysts which opened into bronchi, later becoming air-containing, or finally, whether this picture was produced by a deficiency in connective tissue stroma we are unable to say.

Dr. Douglas H. Sprunt was kind enough to review all the pathological material and to revise the pathological report. The following is his interpretation of this review:

"Our interpretation of this case, both from the history and morbid anatomical findings, is that this is one of acquired pulmonary emphysema, for there is nothing in the history to indicate that he had any pulmonary malformation before the age of 30. There is nothing in the history or anatomical findings to explain why this began to develop at this time. All we have is a case of pulmonary emphysema of unknown etiology, but I do not believe it should in any way be confused anatomically with congenital cystic disease of the lung, although it seems to us that the most likely interpretation is that the elastic tissue of the lung was of a poor quality, and, around 30 years of age, had deteriorated to such an extent that it led to this extensive pulmonary emphysema."

Discussion

There has been no effort to make an exhaustive review of the literature, but there has been an effort to look into the question of cystic disease of the lungs with special emphasis on its congenital form. Various individuals have been given credit for reporting the first case; namely, Fontanus in 1638, Bartholinus in 1687, and Meyers in 1858. However, the first comprehensive report of this condition was made by A. R. Koontz in 1925. At this time he collected 108 cases from the world's literature, and added one of his own. Schenck [1] in 1937 stated that 381 cases had been reported, including five of his own. Francis A. Ford [2] reported a case of a gradually expanding pulmonary cyst in a new-born infant diagnosed by roentgen-ray and confirmed by autopsy.

There are various theories concerning the formation of these cysts. King and Harris [3] offer a rather unique explanation. They quote S. S. Simpkins as saying that the bronchi develop as small ramifications of entodermal tissue which become canalized almost immediately. King and Harris think that an unknown process interferes with this canalization at some point proximal to the termination of that particular ramification, and that this interference results in an occlusion at that point. Beyond this point, canalization begins again, and thus an isolated canalized segment is formed. The mucous membrane of this segment in turn assumes a normal secretory function, and a cyst is formed. Probably the rapidity of the prenatal growth and the size of the cyst at birth are dependent on (1) the amount of functioning bronchial mucosa entrapped, and (2) the capsular strength of the cyst.

The morbid anatomy is described very similarly by various writers. According to Wood [4] all cases fall into two groups: first, those in which there are single or multiple large cysts containing air or fluid; and second, diffuse degeneration resulting in so-called "honeycomb" type of lung. The cysts themselves may be designated as follows: first, fluid cysts; and, second, air cysts. The fluid cyst is one that has not ruptured into a bronchus. There are two types of air cysts—the non-expansile and the expansile. The non-expansile cyst has a small opening into a bronchus, and air is able to get in and out slowly. Harris and King say that according to Jackson, this small opening represents a bipass valve. The expansile, or balloon cyst has an opening into a bronchus through which the air can enter but through which it cannot escape. Jackson calls this mechanism a "check valve." When the opening from the bronchus is large and free, the cyst usually cures itself. Jackson says that all fluid cysts are caused by stop-valve occlusions.

Cole and Nalls [5] state that the cyst walls have the characteristics of bronchi, bronchioles, atria, infundibula, or alveoli. The cysts are often traversed by strands of fibrous tissue which gives them the appearance of being trabeculated. Fluid cysts contain gelatinous or albuminous fluid

which in turn contains desquamated epithelial cells or debris. The wall of the cyst may be thick or thin. This depends on the size of the cavity, the pressure in the cyst, and the presence or absence of infection. Koontz [6] found the small or medium-sized cavities lined with many-layered ciliated columnar epithelium, whereas the larger cavities were lined with flat or cuboidal cells. External to the mucosal membrane are found elastic tissue, concentric fibers of smooth muscle, and pieces of cartilage. The cysts may contain fluid, fluid and air, or only air. An air cyst may involve one whole lobe, or even an entire lung. It may even press over into the mediastinum and embarrass the other lung. This is characteristic of the balloon cyst with its check valve or ball valve mechanism. This type of cyst ruptures easily and may in this way cause a real pneumothorax.

Cystic disease of the lungs may cover the whole span of life, extending from premature stillbirth to very old age. Koontz says that in a patient who has reached maturity, it is hard to tell whether a cyst is congenital or acquired, but he agrees with other authorities that the lack of pigment in the wall of the congenital cyst is the differential diagnostic point. This point alone shows that the pathological condition antedates birth. If the embryological assumption about these cysts is admitted, then all of them begin as fluid cysts. It would seem that the increasing internal pressure and the strength of the cyst wall would be the main factors in determining when the fluid cyst would rupture into a bronchus. W. Anderson [7] advances the theory that in the presence of pulmonary infection, the fluid cysts enlarge rapidly and occasionally rupture. He thinks that a coughing seizure may be a precipitating cause.

Gordan[8] says that if no complication arises, these patients may remain symptom-free for years. The symptoms are usually not diagnostic in character. Authorities, agree, however, that recurring attacks of cyanosis and dyspnea in infants and children should suggest the possibility of congenital cystic lung disease. Wood [9] states that progressive dyspnea with or without preceding infection in an older individual should suggest this condition. He further states that the clinical manifestations of this condition vary greatly, and that their severity depends upon two factors: first, the extent of destruction of parenchymal tissue; and second, the change in intrathoracic pressure. A sudden increase in pressure in a balloon cyst will cause a sudden attack of cyanosis and dyspnea. Expectoration may or may not be a symptom. This depends upon a channel being present between the cyst and the bronchus. Fever is present only when there is infection, and it is seldom very high. Anorexia, palpitation, and vomiting may be present. There may or may not be hemoptysis, and if present, it often raises the question of tuberculosis. Epigastric distress may be marked. There may be great loss of weight. Dehydration and lethargy may be present. Cough may be a marked symptom, and wheezing may occur. In fact, the condition may simulate asthma very closely. Our patient, who

showed many of these symptoms, had been diagnosed and treated as an asthmatic by at least one doctor.

The clinical diagnosis is almost entirely dependent on roentgenology. King and Harris found only one instance in which the clinical diagnosis was made prior to roentgenologic examination. The fluid cysts offer much more difficulty from a diagnostic standpoint than do the air cysts. These cases often give the history of having spat up milky or albuminous fluid. This happens when a fluid cyst ruptures into a bronchus. Kirklin [10] quotes E. F. Pearson as saying that many cases with congenital cystic disease are wrongly diagnosed acquired bronchiectasis, localized emphysema, or pneumothorax.

There are several procedures which may be of help in making the diagnosis. Lung mapping with lipiodol may be helpful. Induced pneumothorax may help. This procedure will often push the cyst wall away from the chest wall, and thus differentiate the condition from pneumothorax. Fluid-containing cysts must be differentiated in the main from the following conditions: (*a*) pulmonary abscess, (*b*) dermoid cyst, (*c*) thoracic tumor, (*d*) echinococcus cyst, (*e*) empyema, (*f*) teratoma, (*g*) chondroma, and (*h*) ganglioneuroma. Freedman [11] says that the solitary giant-type cyst is more common in children than it is in adults; whereas in adults, the cysts are more often multiple in type. A non-expansile air cyst is usually in the intrapulmonary tissue. Schenck says that there may be increased illumination in air cysts during forced inspiration. He also states that emphysematous bullae may be differentiated in that they show no delimiting wall. Pneumothorax shows no wall, and in addition to this is outside the lung parenchyma. The wall of the tuberculous cavity is thickened, and there is usually some tuberculous infiltration about it. The expansile cyst tends to obliterate the lung markings, and at times the findings are not unlike complete pneumothorax. There is often some haziness of the lungs at the apices, and the costophrenic angles may be obliterated. These last findings are due to the atelectasis of the compressed pulmonary tissue. One will notice in the present case report that the obliteration of the costophrenic angles was reported by the roentgenologist as due to fluid.

Mortality is high in children and infants. Infection is a grave complication, especially in the fluid cyst. It has been noted by numerous observers, however, that the condition may be present for many years without producing any symptoms. The case being reported is an example of this. The prognosis in this case was, of course, bad, and it would seem to be due mainly to two factors: first, the small amount of lung parenchyma remaining; and second, increased intrapulmonary pressure.

The treatment of this condition is often unsatisfactory. Cole and Nalls say that treatment is dependent on the size, number, location and type of cysts, the presence or absence of infection, and urgency for relief of symptoms. Wood [9] says that some cases are improved following bronchoscopic aspiration and injection of lipiodol, but he thinks that this treatment

should be limited to infected cysts which are amenable to this type of drainage. Two of his cases had fluid cysts removed surgically. He mentions one case with a large balloon cyst that was treated by thoracotomy and cauterization of the bronchial communication. Following recovery from this operation, the patient lived 10 years, and finally died of some unrelated condition. Schenck advocates extirpation of the cysts, saying that at times lobectomy should be resorted to, but he adds that the procedure is attended with grave danger. Freedman says that no giant air cyst should be tapped unless it interferes with respiration, because this procedure may be followed by shock and death, but it is often necessary to do emergency thoracenteses in these cases to relieve the pressure. According to King and Harris, Adams emphasizes the importance of attaching to the thoracentesis needle a rubber tube and placing its end under water, thus maintaining equalized intrathoracic pressure. They also state that iodized oil should be injected into the cyst at the first thoracentesis. Pearson[12] says that Adams caused stenosis of bronchi in man by applying 35 per cent silver nitrate through a bronchoscope to the bronchial mucosa. Adams has also suggested injecting silver nitrate into the cysts in an effort to destroy the lining epithelium and thus give better opportunity for obliteration of the cavity. Adams also advised using the thoroscope or straight cystoscope in order to visualize and cauterize the bronchial communication. Naturally, if enough lung units are destroyed, there is no surgical or medical procedure which will do any good.

Comment

Our patient was quite uncomfortable; in fact, life was almost unendurable. For this reason, it was decided to try to do something for him surgically. The record shows how unsuccessful we were in this endeavor. It was hoped in the first place to confirm the roentgenologic diagnosis of lung cysts, and in the second place, it was hoped that the opening of the cysts might gradually be blocked by lipiodol, or by nitrate of silver.

From a roentgenologic point of view, this case was typical of that group which has been diagnosed congenital cystic disease of the lungs. But, as Koontz has very correctly said, it is almost impossible to differentiate between congenital cystic disease of the lungs and the acquired form, and in this case we were left in some doubt even at the autopsy table. As will be remembered, lack of pigment is one of the main differential points. In this particular case, there were no fluid cysts; so all the cysts contained air, and naturally contained pigment. Although many of these cysts were on the periphery of the lungs and definitely seemed to be emphysematous bullae, some of them were in the lung tissue. Here, therefore, we have occurring in the lung of the same patient, cysts and emphysematous bullae-like cysts. The roentgenogram of part of the right lung which had been taken in 1932 shows the upper portion of the right lung to be fairly clear except for a few cysts. This piece of evidence would suggest that the cystic condition of

this patient's lung is an acquired one. Although it is impossible to make a definite diagnosis of the etiology, it is certainly logical to suppose that there must have been some fundamental anatomical basis for the cystic disease.

One cannot be sure that all the points mentioned in the pathological report are of diagnostic value. According to this report, the fact that this man had been free of symptoms for 30 years is against there being any pulmonary malformation prior to this time. But various authors state that cases of so-called congenital cystic disease of the lungs may remain symptom-free for years. It would seem, however, that there is a gradual trend to class more and more of these cases as acquired cystic disease rather than as congenital cystic disease of the lung. Pierce and Dirkse [13] say that the term "congenital" is improper in a roentgen diagnosis of cystic pulmonary disease without film evidence of such a lesion at birth.

Conclusion

It has been our purpose, first, to report another case of cystic disease of the lungs; secondly, to emphasize the difficulty of differentiating congenital from acquired cystic disease of the lung; and thirdly, to emphasize the difficulty of doing anything mechanically for this type of case, because any reduction in the vital capacity means the difference between life and death.

We are endebted to Duke University Medical School and Hospital for the pathological transcripts and pictures.

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TULAREMIA WITH PULMONARY COMPLICATIONS *

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Credit for the first clinical description of tularemia is due to R. A. Pearce, a country practitioner of Brigham City, Utah, although only a single reference to his work has been found in subsequent reports of this disease. At the annual meeting of the Utah State Medical Society in Salt Lake City, October 3, 1910, he described six cases which he had observed during 1908, and he stated that he had seen 10 others during 1910. An autopsy on the one fatal case was reported as showing a septic meningitis secondary to a horse fly bite on the face.

The following is an excerpt from his article [2]:

"I will give you the histories of a few cases of an infection probably caused by the bite of a large black and yellow horse fly (sometimes called deer fly) all the cases of which, so far as I know, have been distributed over a definite area about Brigham City. This disease made its appearance in August 1908 and August 1910. The point of infection in all my cases has been on the exposed portion of the body. All the cases give a history of having been bitten by the large black horse fly. Most of the patients say they have been bitten by the same flies many times before during that season.

"The incubation period varies from two to five days.

"In all the cases there has been marked swelling of the glands and lymphatics about the area of the bite. In about one half of the cases some of the glands have gone on to suppuration. Most of the cases have had chills some time during the incubation period, others have chilly sensations. The temperatures have run from 98 to 104° F. The duration of the disease has been from one to four weeks, the severity of the disease varying from slight malaise to death.

"All the bites have gone on from a red infiltration like a mosquito bite to complete breaking down of the tissues and sloughing, forming a punched out circular ulcer about one fourth inch in diameter and an eighth inch in depth. Within a few hours of the bite there forms a water blister at the apex of the infiltration, this soon changing to pus and then the tissue begins to slough away, the discharge being like a seropurulent mucus."

Some important early observations were also made by T. B. Beatty, of the Utah State Board of Health. In 1911 he observed a fatal epidemic among the rabbits in the vicinity of his farm not far from Brigham City, and associated this with an infection of one of his farm hands, resulting from a deer fly bite. As he was unable to obtain cultures from either the

* Read at the Cleveland meeting of the American College of Physicians, April 5, 1940.

rabbits or the patient he sought help from the U. S. Public Health Service. Subsequently, in 1919, Francis identified the disease and the bacterium as identical with the one described by McCoy in 1912.[3]

No pulmonary complications are recorded among the cases observed at the Latter Day Saints Hospital during the first 10 years after the disease was recognized in Utah. The mortality rate in Utah has been very low for tularemia. In 1938 there were 73 cases reported and only one death; in 1939, 44 cases with three deaths. Unfortunately, there was no autopsy report in any of these fatal cases, and pneumonia is not listed as a complication. Of the last 12 cases in the Latter Day Saints Hospital, five have had pulmonary complications. Since only the very sick patients come to the hospital, this proportion of pulmonary complications is undoubtedly higher than occurs in all the cases treated in the home and the hospitals. All four cases that came to our own service in 1938 and 1939 showed pulmonary complications consisting of bronchitis in one, pleurisy with effusion in three, lung abscess with bronchial fistula and spontaneous pneumothorax in one, a unilateral consolidation followed by pleural effusion in one. One of the cases with pleurisy with effusion developed a moderately severe fibrosis and bronchiectasis in one lower lobe.

The diagnosis was made from the history and a positive agglutination test for tularemia. *Pasturella tularensis* was not recovered from the blood or the pleural effusion in any case.

Most of the cases that have occurred in Utah have had contact with rabbits; some have been bitten by wood ticks and deer flies. Unfortunately, many of the rodents and even the sage hens have been known to harbor the infection.

Three of the four cases with pulmonary complications which I am reporting were sheep shearers. Two of them were not aware of any insect bite and had not handled rabbits; this may suggest inhalation as a possible mode of entry.

All four of these cases were treated with sulfanilamide from 60 to 90 grains a day. Additional therapy consisted of transfusions in two cases and convalescent serum in one. All the cases made complete recovery. Two were desperately sick, and for a time it did not seem possible for them to recover. Foshay's serum was not used, partly because it was not immediately available and because we were anxious to test the therapeutic value of sulfanilamide in desperately sick cases. The rapid improvement in the three cases who were able to tolerate the drug well made us feel that it was definitely of specific value.

A brief summary of the essential facts in the four cases is as follows:

Case 1. A. B., male, aged 34, sheep shearer, reported having removed many wood ticks daily from his body and had also dressed a wild rabbit several days before onset. His illness began on May 2, 1938, with a severe backache. On May 5, 1938, he became acutely ill with generalized aches and pains, sweats, fever and pleural pain in his left

chest. These symptoms lasted three weeks. He gradually improved and was up and about for one week. About June 1, 1938, he became acutely ill again with fever, severe cough and pain in his left chest. He remained very sick all through June. About June 22 he felt something break in his chest, and he estimated that he coughed up about one quart of foul sputum in two days. On June 29 he was brought to the Latter Day Saints Hospital. Examination revealed evidence of a pyopneumothorax in the left chest with abscess in the left lower lobe which had undoubtedly opened into a bronchus. He had lost 63 pounds and looked very sick, thin and dehydrated.

Laboratory findings showed: Hemoglobin 78 per cent, red blood cells 4,240,000, white blood cells 16,200 with 70 per cent polymorphonuclears. Agglutination test was strongly positive for *B. tularense*.

Treatment consisted of forced feedings and postural drainage without appreciable change in temperature which ranged from 99 to 102.2° F.

July 1. Sulfanilamide was started in 10 grain doses every four hours.

July 3. Temperature reached normal for the first time and did not exceed 100° F. in the next 10 days. During the following 10 days it barely reached 99°. He was given two transfusions, additional artificial pneumothorax and postural drainage.

July 31. He was discharged much improved.

August 11, 1938. He had gained 19 pounds, abscess in lung was rapidly healing, and he was feeling almost well.

September 26, 1939. Further observation showed him to be apparently cured. Roentgen-ray revealed some thickened pleura and limitation of excursion of outer part of left diaphragm but otherwise essentially normal. He had been working for a month.

Case 2. C. H., male, aged 37, farmer.

June, 1938, he was bitten by a wood tick. This was followed in a few days by a sickness of three weeks' duration consisting of chills, fever, sore throat, general aches and pains. He gradually improved but had recurrent attacks of sore throat and cough all summer.

In September he had an attack of chills, fever, cough and pain in his right chest and a desquamating eruption on his hands.

November 28, 1938, he came to the Clinic complaining of cough with copious sputum, weakness, and loss of weight. He had not been well since his attack in September. Examination revealed fluid in his right pleural cavity, thickened pleura, and many râles. Paracentesis was done, and a straw colored clear fluid was obtained which yielded a sterile culture. It and the sputum were negative for tubercle bacilli. Agglutination for tularemia was strongly positive. He was given sulfanilamide, 40 grains to 60 grains daily, for most of two weeks. The temperature came to normal rapidly and it remained normal. He gained 15 pounds in two weeks. He reported in February that he had continued well since his last examination in December.

Case 3. F. S., male, aged 24, sheep shearer. He often found ticks on his body but was not aware of any bites and had not handled any rabbits or rodents. Two weeks before admission to the hospital on June 28, 1938, he became sick with chills, fever, general aches and pains, weakness, nausea and vomiting.

Examination revealed several sores on his forearms which he called grease sores. Temperature was 102° F., pulse 100. He had dullness and many coarse râles in both lower lobes and the right middle lobe, but no definite consolidation. Spleen was palpable. Roentgen-ray film showed slight cloudiness of the lower part of both lungs. Agglutination test was strongly positive for tularemia and moderately so for undulant fever. He was kept under observation for two days without medication. His temperature ranged from 101 to 103°.

July 1, sulfanilamide was started in doses of 10 grains every four hours. The highest temperature in the next 24 hours was 101°, and during the following 24 hours

it reached only 99.2°. From that day on it remained normal, and all his symptoms and physical signs disappeared with his fever. He made a rapid recovery.

Case 4. C. O., male, aged 62, sheep shearer. He was not aware of any insect bites and had not had any contact with rabbits or rodents.

June 1, 1939, he became suddenly ill with nausea, vomiting, diarrhea, chills and fever, general aches and pains and these symptoms continued with increasing severity until he entered the hospital on June 6, 1939. He appeared very sick, dehydrated and delirious. The temperature was 103° F., pulse 90. He had a severe cough. Examination revealed moderate cyanosis and dyspnea, dullness in left lower chest with diminished respiratory murmur and many râles. The following day there was definite consolidation in his left lower lobe. He was deeply intoxicated and continuously delirious. Cyanosis and dyspnea increased. All the agglutination tests were negative until June 19 when he showed positive agglutination for tularemia. His leukocytes ranged from 6200 to 10,900. His course was a very stormy one and on several occasions his prospects seemed almost nil. After the consolidation cleared, he developed fluid in the pleural cavity which was aspirated on July 3 and 10. A clear straw colored fluid, in amounts of 1000 c.c. and 425 c.c., respectively, was removed. Culture from this fluid remained sterile.

His therapy consisted of sulfanilamide whenever he could tolerate it, forced feedings by nasal tube, intravenous glucose, transfusions and injections of convalescent serum from a man who had recently recovered from tularemia. Recovery was slow but complete. Just what part of his therapy deserved most credit for his recovery it was impossible to tell.

Comment

Clinical cases of tularemia have been known to exist in Utah since 1908. Most of the earlier cases were of the ulceroglandular type.

Pulmonary complications are either more frequent in recent years or they are more often recognized.

It is possible to acquire the disease by handling infected wild rabbits, many other rodents and some of the larger animals. Unfortunately the disease has also been found in the sage hen and the quail.

Next to the handling of infected rabbits the commonest source of the disease is through the bites of wood ticks and deer or horse flies.

The frequency of the infection with pulmonary complications in sheep shearers who have not, to their knowledge, been exposed to the usual source of infection suggests the possibility of inhalation as the mode of infection.

The mere fact that all of our cases with pulmonary complications recovered after receiving sulfanilamide does not prove it to be a specific. The complications may have been owing to a secondary infection, but such organisms should have been easily recovered in the cultures made. The mortality rate in all cases of tularemia is low, but at least half the cases that die have pulmonary complications. The favorable response to sulfanilamide was so immediate and the patients had been sick so long that it precludes the possibility that the results were just a coincidence.

Our conclusions were that the drug has definite therapeutic value in tularemia.

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CHRONIC ULCERATIVE COLITIS—ALLERGY IN ITS ETIOLOGY *

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THE possibility that chronic ulcerative colitis is the most severe result of colonic allergy should receive serious consideration. In the literature,[1] many instances of colonic allergy are reported. Simple colitis associated with varying degrees of diarrhea, abdominal soreness, cramping, tenesmus and mucus frequently is due to specific food allergies. Wheat, egg, milk, fish, honey, various vegetables, fruits and other foods and condiments have been incriminated. Milk allergy, especially, is a common cause of colitis. Two of my patients who had allergic colitis from milk required only a few teaspoonfuls of milk as a laxative. Friedenwald [2] studied a patient with diarrhea of six months' duration due to milk allergy, in whom hydrochloric acid by mouth given because of achylia had failed to bring relief. Cardon [3] recently reported five cases of colitis with varying degrees of cramping, tenesmus, abdominal soreness and diarrhea due to milk allergy. It is generally agreed that the colic of infancy and other gastrointestinal symptoms of childhood may be due to allergy. In mucous colitis and in the unstable or irritable colon, allergy is so likely to occur that it should always be considered as one of the possible causes. The obvious psychoneurotic tendencies in allergic patients may be due to frustration because of the long-standing unrelieved symptoms or to actual cerebral or nervous tissue allergy.[4] Gastrointestinal allergy also may result in symptoms and findings suggestive of appendiceal or gall-bladder disease, of acute or chronic intestinal or colonic obstruction and of organic disease of sigmoid and rectum. Local passive transfer in the rectal mucosa in man has been reported by Gray and Walzer,[5] and of the stomach, small and large intestine, peritoneum, spleen and uterus in the rhesus monkey, by Walzer, Gray, Strauss and Livingston.[6] Pruritus ani sometimes is a mucosal inflammation with cutaneous dermatitis arising from allergy.

These colonic symptoms arising from allergy differ in variety and degree because of allergic reactivity. Varying amounts of allergic mucosal inflammation with serous or mucoid secretion, and generalized mild or severe localized edema, the latter causing signs of obstruction, may occur. Increased vascular permeability is frequent, causing easy bleeding of the mucosa and at times frank hemorrhage, as recently reported by Rubin [7] in infants with colic. Smooth muscle spasm, which frequently is the result of allergy, may also occur accompanied by cramping, pain and tenesmus.

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In chronic ulcerative colitis, the foregoing allergic reactions may explain the presence of erythema, of the granular type of mucosal inflammation with varying capillary bleeding, and of serous or mucoid secretion. Andresen [8] is of the same opinion. Such tissue reactions may be similar to those responsible for atopic dermatitis which is characterized by cutaneous erythema, minute papulo-vesicular lesions, thickening, exfoliation, oozing and crusting with secondary infection in varying degrees. Ulceration, denudation of the mucosa, and infection of the colonic tissues may be absent or they may be so severe that septicemia or perforation of the bowel results. Two explanations of the origin of ulcerations are offered. First, if a superimposed infection from colonic bacteria, especially streptococcus, arises, localized ulcerations may develop and produce cellulitis, fever, purulent discharge and subsequent formation of scar tissue, fibrosis and contraction of tissues. Ulcers may vary from the superficial mucosal to the deeper, larger, more penetrating type depending on the patient's resistance to the infection. Second, the ulcerations may arise from localized vascular allergy as do canker sores in the mouth, which allergists agree are usually due to food and less often to drug and bacterial allergy. Similar canker-like recurrent ulcers due to food allergy have been observed in the vulva and vagina of one of my patients. The rôle of allergy in the etiology of peptic and corneal ulcers has long received consideration in the literature.[1] Also the tendency to polyp formation suggests allergy as the cause. Practically all the polyps that arise in the nasosinal mucosa are due to allergy, and polyposis in the stomach has occurred in some definitely allergic patients.

Thus, chronic ulcerative colitis in all its stages may be caused primarily by allergy and secondarily by superimposed infection and the effects of resultant avitaminosis.

In cases in which food allergy is the cause, the tissue reactions may arise from blood-borne allergens absorbed from the stomach or small intestine or from food allergens absorbed from the colonic content itself which might produce a contact-like reaction. The latter is possible because of the rapidity with which ingested foods, usually inadequately digested, reach the colon in cases of diarrhea.

Furthermore, the recognized characteristics of clinical allergy may explain some of the characteristics and variations of chronic ulcerative colitis.[1] Allergic reactions are localized in various tissues. Thus, alimentary allergy may be present only in the mouth, in the stomach, in part of the small intestine, in the cecum, in the sigmoid or rectum, or in restricted or large areas of the colon. After it has been established, it tends to extend to larger areas. Regional enteritis, especially in the ileum, should be studied from the allergic point of view. The recurrent attacks of asthma, migraine or urticaria frequently may result from refractoriness or hyposensitization of the shock tissues. Anergy or [9] failure of tissues to react allergically also may occur. These observations may explain why remissions and variations in symptoms arise in certain patients with chronic ulcerative colitis.[8] The re-

ported beneficial effects on food allergy of the summer months and of residence away from the ocean,[10] especially in dry inland areas, also may explain some of the variations in colonic symptoms. Other environmental and seasonal influences have been observed especially in inhalant allergies (Case 2).

Clinical Studies

Andresen [8] first reported food allergy as a cause of ulcerative colitis.* One patient had a return of bloody, mucoid dysentery from eight drops of milk concealed in his food the night before.

Hare,[11] in 1935, found that 85 per cent of 38 patients with chronic ulcerative colitis had definite family or personal histories of allergy. She noted its occurrence in adolescents and young adults, especially in females, and its precipitation by acute infection.

Mackie,[12] in 1938, maintained that the relation of chronic ulcerative colitis to allergy, particularly to food allergy, requires study. Since skin tests failed to demonstrate clinical sensitizations to food in most instances modified elimination diets of the writer were used to study possible food allergy. Of 67 cases thus studied, definite indications of food allergy were noted in 44 and equivocal evidence in seven. Milk, egg, orange, wheat, spinach, and tomato named in the order of frequency, headed the list of allergenic foods. Evidence of bacterial allergy also was noted. Mackie emphasized the frequency of avitaminosis, hypoproteinemia, and loss of weight owing to improper utilization of ingested foods.

Personal Studies

Cases 1 and 2. In December of 1937, two patients reported because of perennial nasal allergy and looseness of the bowels. One of these, a woman aged 35, had suffered from nasal and bowel symptoms all her life. Diagnosis of ulcerative colitis had been made. The possibility of infectious and parasitical colitis had been investigated and psychoneurosis had been considered. With fruit-free elimination diets her nasal symptoms and the looseness of bowels had been entirely controlled for the last three years. Milk in small amounts rapidly caused nasal congestion and diarrhea.

The other, a man, aged 29, had had similar nasal and bowel symptoms for 14 years. He had had bronchial asthma all his life, although it had improved the last 10 years. A brother had asthma and a sister had colitis. As amebae had been found on one occasion the patient had been treated with anti-amebic drugs. Colonic irrigations, and injections of thiamin and liver had been used. Diagnosis of ulcerative colitis had been made by roentgen-ray and by repeated proctoscopic examinations. During the past three years, on a diet eliminating milk and several fruits and vegetables, the colitis improved definitely. We believe that better results would be obtained if the patient adhered more strictly to the diet. Because of his positive skin reactions and the seasonal exaggeration of his nasal allergy, pollen therapy also was administered.

Case 3. In September of 1938, a man, aged 28, who had chronic ulcerative colitis of four months' duration was first seen at the Alameda County Hospital. He had had loose stools, up to 20 a day, with varying amounts of blood, mucus and pus as well as

* Since acceptance of this article, Andresen has published: Ulcerative colitis—an allergic phenomenon, Am. Jr. Digest. Dis., 1942, ix, 91.

frequent incontinence. His temperature varied from 99° to 102° F., and his weight and strength were markedly impaired. Diagnosis had been made by proctoscopic and roentgen-ray studies. The patient had always disliked milk. No other indications of allergy were noted. This was his first illness. Skin reactions to all ingestant and inhalant allergens by the scratch test were negative. Stool examinations for parasites and cultures for bacillary dysentery were negative. Therapy with emetine for 14 days and with liver extract and thiamin every three days for two weeks hypodermically had failed to help. Metaphen by vein had been given for two weeks.

On a fruit-free and cereal-free elimination diet in soft, liquid, minced or pureed form, the bowel movements were reduced, within two weeks, to four to six in 24 hours, and the blood and mucus in the stools were reduced. One month later the patient had only two to three formed stools daily. In the last two years, he has had one to two formed stools in 24 hours, entirely free of blood and mucus. Proctoscopic examinations at frequent intervals revealed no ulcers or mucosal inflammation for the last two years. In May 1939, the patient ate a small piece of chocolate cake; within four hours looseness of bowels developed which persisted for 24 hours. Grapefruit, lemon, cooked pears, peaches, apricots and eggs were added to his diet. Because of the possible history of milk allergy and because of the importance of preventing a return of the colitis, milk was not given. At the last observation the patient felt well. In the last three years he did not lose a day's work in a steel mill because of illness. He weighed 50 pounds more than when he was first seen.

We believe that food allergy, especially to milk and probably to wheat, was the major cause of the ulcerative colitis in this case. The rapid improvement during the first month of dieting, the long-standing dislike for milk and the definite diarrhea after eating cake confirm this assumption. Furthermore, we believe that the injections of thiamin and liver extract (as suggested by Cheney [13]), for 10 months, two to three times a week after the patient left the hospital, relieved probable avitaminosis, and that neoprontosil by mouth (as suggested by Brown, Herrell and Bargen [14]) in two courses, in the first six months after hospitalization, may have discouraged persisting secondary infection. No medication had been given for two years prior to the last observation. The bowel was then normal by proctoscopic and roentgen-ray examinations.

Case 4. A man, aged 32, observed in the Medical Clinic of the University of California Hospital, had been suffering from chronic ulcerative colitis for five years. Proctoscopic examination revealed a red, glistening mucosa with adherent mucus and many small ulcerations. The roentgen-ray showed absence of haustra in a narrowed descending colon. Watery movements, at times streaked with blood and containing mucus, had numbered 12 to 20 a day for several years. Loss of weight and strength was marked. No cause had been found for the diarrhea after careful laboratory tests of all types. The patient was placed on a cereal-free and fruit-free elimination diet; all the foods were cooked, pureed or minced. In two weeks the diarrhea had decreased. Since then (in two and a half years) the stools declined to two to four a day; they usually were semi-formed. The patient gained 18 pounds in weight, and his strength and energy returned. At last observation he was eating beef, lamb, liver, tongue, chicken, white and sweet potato, most of the vegetables (still cooked but no longer pureed), pears, peaches, tapioca, sugar, sesame oil and salt. He received daily 50 mg. cevitamic acid by mouth. Tea and soy-lima bread produced diarrhea. Other foods commonly productive of allergy had not been tried in his case.

Case 5. A man, aged 61, developed diarrhea in late September, 1940. The next day watery, bloody movements with severe tenesmus and a fever up to 102° F. were present. Agglutination tests on the blood serum, stool cultures, and microscopic examination of the stools offered no explanation for the diarrhea. Finally a roentgen-

ray picture of the barium filled colon showed typical ulcerations in the sigmoid and parts of the ascending and transverse colons. Proctoscopic examination showed superficial ulcerations and a congested, easily bleeding mucosa with some adherent bloody mucus. Microscopic examination of a piece of the rectal mucosa showed many eosinophiles. The personal and family history of allergy was negative. There was no history of any idiosyncrasy or dislike for foods. Skin reactions with the scratch test to food allergens were negative.

A diagnosis of acute ulcerative colitis was made and a cereal-free and fruit-free elimination diet was prescribed. All foods were cooked, pureed, or minced and given in small amounts at frequent intervals. Immediately stools reduced in number.

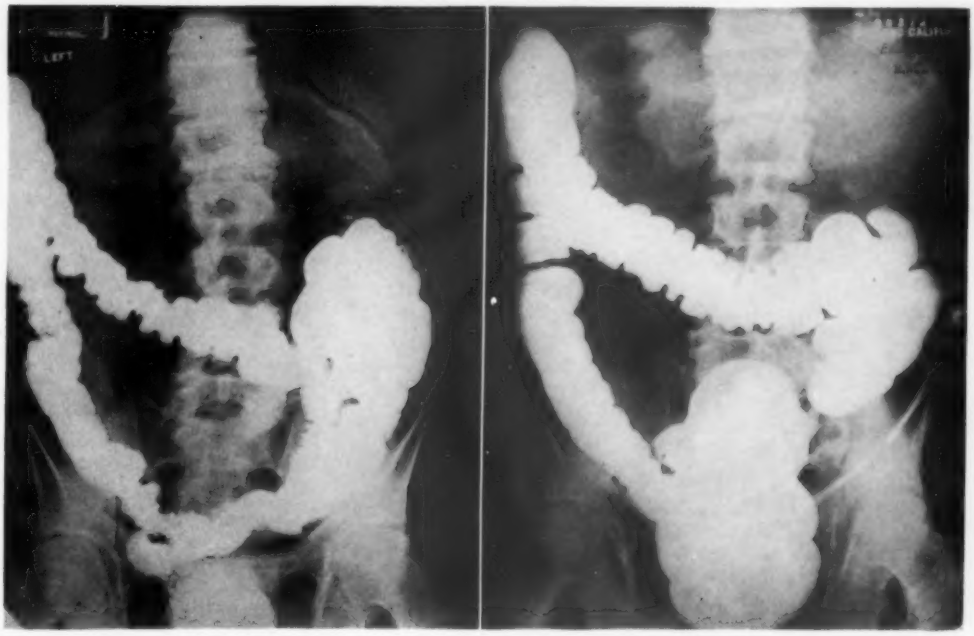

FIG. 1 FIG. 2

FIGS. 1 and 2. Roentgen-ray pictures of the colon of Case 5. The typical ulcerations in the sigmoid and transverse colon are shown in figure 1. The normal colon four months after the elimination diet was instituted is shown in figure 2.

In four or five days only three or four stools devoid of blood and mucus were passed, and in 10 days his normal bowel activity had returned. Rice, corn, rye, eggs, fish, fresh grapefruit and lemon, cooked pears, peaches, apricots and prunes were gradually added, and in the last six months all other foods were tried. Each time milk was taken cramping and diarrhea developed in a few hours. His colon was normal by proctoscopic and roentgen-ray examinations.

Case 6. A woman, aged 31, was seen in January 1941 with a history of chronic ulcerative colitis of six years' duration. Liquid to soft stools, varying from six to 20 daily, with intermittent blood and mucus, cramping, tenesmus and abdominal soreness and moderate fever had been present since 1935. Much abdominal soreness and pain, especially in the right side, had occurred. Weight had fallen 50 pounds. Fatigue and somnolence had been present for four years before colitis had developed. The mother had had sick headaches for years, and the patient had frequent nasal congestion.

Proctoscopic and roentgen-ray examinations had indicated chronic ulcerative colitis. Treatment with bland diets, oral vitamins, tincture of opium, liver and iron injections, autogenous stool and Bargen's vaccines had been of no benefit.

Moderate nasal congestion suggested possible allergy. The patient had been susceptible to prolonged head colds with fever since her teens. Her dietary history revealed no food dislikes or disagreements, except that crab produced diarrhea. Alcoholic beverages and tobacco smoke produced cramping and diarrhea. Skin reactions by the scratch tests with all important foods and inhalants were negative.

The patient was placed on a cereal-free and fruit-free elimination diet, consisting of soft, pureed, liquid or minced foods. Within one month she had two to three formed stools every 24 hours and was free of urgency and incontinence. At the last observation she had one or two formed stools daily. All abdominal and bowel symptoms were gone. Constipation might occur. Her strength, energy and appetite increased. For the first time in 10 years she was doing her own work.

She received by mouth synthetic vitamin C, thiamin, riboflavin, pantothenic and nicotinic acids, viosterol, and calcium carbonate. Repeated trials showed that corn, sweet potato, tomato, onion and peaches caused diarrhea. Eggs were tolerated. Milk and wheat were not tried because of the excellent results obtained and because of my desire to prevent any marked allergic reaction in the colon.

Case 7. A man 22 years of age developed intermittent cramping and diarrhea in 1938. During the following year, these symptoms increased in degree and frequency and blood often was noted in the stools. In 1940 he had loose stools six to 10 times every 24 hours with blood, at times in large amounts. Fatigue, weakness and nervousness were marked. No treatment was given except retention enemas and local rectal applications. On a soft smooth diet with extra milk, his symptoms steadily increased.

We first saw this patient in the Medical Clinic of the University of California Hospital. Roentgen-ray and proctoscopic examinations showed definite ulcerative colitis. Stool examinations for parasites were negative. He had had no colic or feeding disturbances in childhood, but had been troubled with constipation all his life for which he had often taken laxatives. He had had recurrent bronchitis from the fall to the spring months up to the age of 17. One attack of asthma occurred five years previously. Moderate nasal congestion and "catarrh" had been present for years. His father had had constipation and distention for many years and rheumatic pains and soreness for 10 years. The patient gave no history of food idiosyncrasies or dislikes.

In January 1941, he was placed on a fruit-free and cereal-free elimination diet in soft, minced or liquid form. In three weeks he had only three soft, semi-formed stools without blood in 24 hours. Since then he had one or two formed stools in 24 hours without cramping, abdominal soreness or blood. He gained 15 pounds in spite of constant hard work; and his weakness, fatigue and nervousness entirely disappeared. He reacted to milk with definite diarrhea and cramping. He tolerated eggs. His reaction to wheat was in question.

Case 8. A man aged 38 had had frequent loose stools and cramping, with blood and mucus, for four years. Beginning in June 1939 he had two to three watery movements daily with an increased amount of blood and mucus. Proctoscopic examination showed an inflamed mucosa with many small irregular superficial ulcers. During the following seven months he was in three different hospitals. Therapy consisted of three transfusions, administration of vitamin and of liver, and other dietary and medical treatment. An ischiorectal abscess and anal fistula developed. Fever and continual bloody diarrhea persisted. Gradually the patient improved and in May 1940 he returned to work. However, easy fatigue, weakness, abdominal soreness, cramping and bowel urgency, with four to six semi-watery stools, persisted.

In March 1941 these symptoms increased and the patient entered Highland Hospital on May 30. Proctoscopic and roentgen-ray studies showed a reactivated chronic ulcerative colitis from the hepatic flexure to the sigmoid. The patient had a temperature up to 101° F., watery stools up to 16 per day with much incontinence, blood, pus and mucus, and loss of weight, strength and appetite. Sulfanilamide and later sulfaguanidine, thiamin and liver given parenterally and two transfusions produced no definite benefit.

On July 17 a cereal-free and fruit-free elimination diet, consisting of soft, liquid, minced or pureed foods, was instituted. In three weeks the patient had only one to two semi-formed stools with no blood or mucus each 24 hours. The fever disappeared, and appetite and strength increased. Since then formed stools continued, the patient's weight increased 34 pounds, and he was at work on an automobile assembly line for three months. His strength and health were better than in six years. Recent proctoscopic examination by Dr. P. J. Dick showed extensive plaque-like healed scars several centimeters long. The adjacent mucosa in places was edematous, but no polypi, bleeding, oozing or ulcerations of the mucosa or decrease in the size of the intestinal lumen were seen.

This patient's family and personal histories of allergy were negative. Scratch tests with foods were negative. There was no history of food dislikes or idiosyncrasies.

Case 9. A boy eight and a half years of age had passed blood-streaked stools every few months since May 1938. Before entering the Children's Hospital in Oakland in August 1941, he had passed loose or liquid stools with increasing amounts of blood and mucus three to six times each 24 hours for eight months. Urgency and incontinence often had kept him out of school. For three years increasing fatigue, irritability, loss of appetite and recently afternoon temperature up to 102.5° F. had been present. Physical examination was negative except for a scaling and thickening of the skin around the mouth, a facial tic, and diffuse moderate soreness of the abdomen on palpation. Blood and urine analyses were normal. Stool examinations showed much blood, pus and mucus but no parasites. Stool cultures and serum agglutinations were negative for bacterial causes of dysentery. Proctoscopic examination showed an edematous, granular mucosa with mucopurulent discharge. Roentgen-ray studies of the colon showed poorly developed haustrations in the descending colon and sigmoid, and a diffuse fine irregularity of the mucosa.

A fruit-free and cereal-free elimination diet in soft, liquid, minced or pureed form was started on September 9. Blood and mucus disappeared in a week. In two weeks the patient passed a soft or semi-formed stool only every one to three days. Within one month the stools became formed. On September 16, because of continued afternoon fever, sulfathiazole was given in doses of 60 grs. daily for one week, followed by 40 grs. daily for nine days. The temperature became normal in three days, remained normal for nine days, but again rose to 101° or 102° F. during the last four days of administration of this drug. Since the fever continued for five days, sulfaguanidine in doses of 60 grs. daily for one week and 40 grs. for two weeks was given. The temperature remained below 100° F. by rectum after October 13. Since mucosal infection was assumed to be the cause of the fever, increasing doses of Bargen's streptococcal vaccine and of stock respiratory organisms were administered at first every two to three days and then every five to seven days.

For the last three months the bowels were normal with no blood or mucus; appetite, strength and energy increased, no fever was present, and the facial tic and dermatitis around the mouth disappeared. The patient gained 12 pounds in weight. Rice, corn and rye, egg, pear, peach, apricot and celery were added to his original diet. His foods were cooked in the usual manner without pureeing or mincing. He was taking one teaspoonful of calcium carbonate a day and viosterol in sesame oil, 10 drops daily. Recent proctoscopic examination revealed a slightly granular mucosa but no ulcerations or points of bleeding.

Case 10. A man, aged 25 years, had had diarrhea with blood and cramping for two weeks in July 1935. The cramping recurred for one to two hours for one to two days every one to three weeks until July 1936. At that time severe, bloody diarrhea with fever set in, apparently after ingestion of strawberries. The patient was in the hospital for 24 days. Milk disagreed with him. From November until May 1937 he had four to six loose stools daily with occasional blood. The symptoms continued in varying degree until July 1940 when after drinking much loganberry juice, his most severe bloody diarrhea with mucus and cramping developed. Sulfanilamide gave no relief. Upon diet trial ordered by Dr. J. E. Hunter of Seattle the colitis has definitely improved. In order of harmfulness the following foods have been incriminated: nuts, berries, pepper, cabbage, cauliflower, corn, beer, coarse bread and vegetables, sweet potato, alcohol in excess, raw fruits and vegetables, and milk. The patient had known that potato and milk caused "gas." He had had no allergic diseases in the past except occasional hives. His family history revealed that his mother had hay fever and "sick" headaches. A maternal aunt and grandmother had had "sick" headaches. The father had had boils on his face after eating pork.

In October 1940, Dr. T. T. Mackie informed me of a case of seasonal ulcerative colitis recurring each year during the ragweed season. Marked relief occurred in an air conditioned room, and a severe exaggeration of the colitis resulted from the hypodermic administration of ragweed pollen. A similar case studied in the last 14 months follows and is the first published record of complete relief from pollen therapy.

Case 11. A woman aged 43 who was seen in the Clinic of the University of California Hospital in September 1940, had had chronic seasonal ulcerative colitis since 1931. Watery or loose stools with blood and mucus associated with moderate fever varying in degrees, weakness, malaise and dull or cramping pains in the lower abdomen recurred each year during July or August and lasted until November or December. She had been first seen in the clinic in September 1934. At that time a proctoscopic examination had revealed a granular and hyperemic mucosa with many small ulcerations and bleeding areas. Since then other proctoscopic examinations during the autumn months had confirmed the diagnosis of "idiopathic" ulcerative colitis. Stool examinations for parasites had been negative. Stool cultures in 1936 had yielded hemolytic *Bacillus coli, Staphylococcus aureus* and alpha hemolytic streptococcus from which vaccine, lysate and bacteriophage were made. The vaccine given subcutaneously, the phage by mouth, and the lysate applied to the rectal mucosa, had yielded no definite results.

As a child the patient had had croup. "Sick" headaches had recurred for many years especially during menstrual periods. Mild hay fever in the fall had recurred from 1918 to 1923 in Chicago. Her dietary history was negative except that for years eggs had caused belching. Her family history was unknown.

In September 1940, she was tested by the scratch and intradermal methods with all inhalants including all important pollens of this area. Negative reactions resulted except for a one-plus reaction to Red top and Curly dock pollens. However, because of the seasonal recurrence of her colitis, an antigen containing ray, bermuda, mugwort, coastal sage, rough pigweed, white goosefoot, false ragweed, Russian thistle and pickle weed pollens was prepared and administered from the fall of 1940 until the time of this report. For the first time in 11 years no symptoms whatsoever developed in the fall of 1941. Her blood counts were as follows:

	9/28/40	1/28/41	4/29/41
White blood cells	15,050	10,500	11,600
Eosinophilic neutrophiles	22%	6%	1%

Patients Uncontrolled through Allergic Study

During the last two and one half years four patients with chronic ulcerative colitis have failed to respond to elimination diets.

Case 12. A woman 34 years of age entered the University of California Hospital on March 31, 1939. Cramping and diarrhea, with some blood, had first occurred for one week in August, 1938. By mid-December 10 to 15 watery stools a day with blood, pus and mucus had developed and persisted. Increasing weakness, fatigue, anorexia, anemia and loss of weight had been present. Six weeks previously a chill had occurred and a daily temperature up to 101° to 104° F. had continued since then. No parasites or positive agglutinations were demonstrated. Proctoscopic examination showed severe ulcerative colitis. Previous treatment had included intensive administration of vitamins A, B, C and D; emetine and carbazone; high caloric diets; calcium gluconate by vein; five blood transfusions; reticulogen in doses of 1 c.c. daily for two weeks; sulfanilamide and sulfapyridine by mouth; tincture of opium (for cramps); and Bargen's vaccine hypodermically.

On April 13, a cereal-free and fruit-free elimination diet was instituted. In three days the stools were less frequent. However, a rectovaginal fistula had developed three weeks before and the apparent improvement was terminated by perforation of the sigmoid with resultant shock, peritonitis and death two days later. Autopsy revealed acute ulcerative colitis with perforation of the sigmoid, pelvic abscess, rectovaginal fistula, acute ulcerative esophagitis and fatty degeneration of the liver.

Case 13. A man 20 years of age was first seen in the University of California Hospital in September 1940 with chronic ulcerative colitis. Diarrhea with mucus and blood had gradually developed in 1934. Since then bland diets, Bargen's and autogenous vaccines, and carbazone had been given. Periods of improvement and prolonged exacerbations had recurred but the symptoms had persisted. Since January 1940, loose stools up to 14 a day, with blood, pus and mucus associated with intermittent fever, had continued. Sulfanilamide by mouth, and thiamin and liver extract parenterally had failed to improve the condition.

On October 22 the patient was placed on a cereal-free and fruit-free elimination diet. In addition thiamin and liver extract intramuscularly, dilute hydrochloric acid with feedings, vitamin C, viosterol and calcium gluconate by mouth were given. In two weeks the patient felt better. The mucus and blood in the stools had diminished, but the diarrhea and fever continued. In spite of other elimination diets his symptoms, especially the fever, persisted, and septicemia was suspected. Blood cultures, however, were negative.

On December 9 Dr. Leon Goldman did an ileostomy, soon after which, on a high caloric diet, the patient's weight and strength increased and the fever disappeared. In spite of this improvement and diversion of the fecal contents through the artificial opening, blood, mucus and pus continued to be passed per rectum. On July 2, 1941, Dr. Goldman did a colectomy. Recovery was rapid. The patient's strength increased, and his weight increased 60 pounds since the first operation.

Case 14. A man, aged 50, who was first seen in the Medical Clinic of the University of California Hospital in July 1941, had had chronic ulcerative colitis for four and one-half years. For the first one and one-half years, five to six soft or watery stools in 24 hours recurred for one to three weeks every one to two months. In the last three years bright blood with some mucus had varied in degree, and recurrent colitis had prevented the patient from working. Various diets and medications had been of no benefit. Proctoscopic examination revealed a red, angry-looking, granular mucosa which bled freely in small areas. A great-aunt had had asthma. The patient had had frequent gastrointestinal upsets with vomiting in childhood.

On July 29, 1941, a cereal-free and fruit-free elimination diet was instituted. In 12 days the patient passed stools less liquid with fewer flecks of blood every two to four hours. In addition to the diet, B vitamins, cevitamic acid and calcium carbonate by mouth and liver extract intramuscularly were given. On August 12, stools had declined to six to eight a day, were soft, and showed only a few traces of blood. The patient felt he was stronger but his appetite remained poor. Because of a moderate anemia, the flecks of blood in the stools, and a slight fever, he was hospitalized.

Neoprontosil and later sulfanilamide by mouth were of no benefit. His weight and appetite decreased, possibly due to the drug therapy. The elimination diet was displaced by a high caloric bland diet. Sulfaguanidine was administered together with thiamin and liver intramuscularly. The patient was discharged from the hospital unimproved and ileostomy with subsequent colectomy was advised.

Case 15. A man 30 years of age had had intermittent rectal bleeding attributed to hemorrhoids in 1936 and 1937. Since then varying degrees of diarrhea with blood, mucus and pus, and a temperature up to 104° F. had persisted. Proctoscopic and roentgen-ray studies had revealed chronic ulcerative colitis. Vitamin B and liver extract, vitamins A, B_1, riboflavin, nicotinic acid, vitamin D and yeast had been given in large amounts by mouth. Sulfathiazole, sulfanilamide and sulfaguanidine by mouth, retention enemas of various medications, various diets and vaccine therapy had been of no benefit. An ileostomy had been done eight months previously. Since his bowel symptoms and fever continued, a fruit-free and cereal-free elimination diet was tried for four weeks, at the request of Dr. F. B. Taylor, without evident benefit. Thereafter a colectomy was done which was followed by satisfactory recovery.

A history of infantile eczema in the first year of life, of feeding difficulties, constipation and malnutrition had suggested possible food allergy. Nasal congestion with postnasal mucus had been present for several years. Moreover, the mother had had angioneurotic edema from meat, milk and wheat allergy.

Suggested Allergic Study and Treatment

A routine investigation of chronic ulcerative colitis from the allergic point of view is important. For the study of possible food allergy, we have used a modification of the cereal-free and fruit-free elimination diet.[15] When frequent liquid stools are present, the foods should be liquid, soft, pureed or minced. Foods which infrequently cause allergy are included. Fruits are excluded until improvement has occurred. Beef is also excluded at first because of allergens common to beef and milk, the latter food being a frequent offender in this disease. If skin testing is done by the scratch tests and positive reactions to any food are definite or if there is a history of definite idiosyncrasy to any food in the diet, a substitute non-reacting food is used. However, the fallibility of the skin test must be kept in mind. When intolerance or allergy to legumes is evident, rice or additional potato may be used. Protein metabolism should be protected with an adequate intake of prescribed meat or soy bean, the latter being the only vegetable source of all amino acids necessary for human nutrition. Homogenized lamb, as well as beef and liver,* may be combined with pureed vegetables, soy bean or split pea.

* Prepared by Clapp & Co., Rochester, N. Y. Not available until after the war.

The following diet is recommended and may be modified as suggested:

CEREAL-FREE AND FRUIT-FREE ELIMINATION DIET

(Liquid, Soft, Pureed or Minced)

Tapioca cooked with sugar, with or without soy bean milk, or with maple syrup or caramelized sugar

White or sweet potato—boiled, baked or riced, served with sesame or soy bean oil and salt.

Lamb-chops, roast or tongue, minced or ground at first, cooked with salt but without butter or other seasoning. Homogenized lamb may be combined with prescribed vegetables.

Soy bean puree—best made from canned cooked beans or from cooked soy bean flour. (Split pea puree may also be used.)

Carrots, beets, peas, squash, artichokes (fresh cooked or canned), strained or pureed. Salt, soy bean or sesame oil may be added but no butter or other ingredients.

Breads [15] made of soy, lima, potato or tapioca flours. Soy bean butter, carrot preserves or maple syrup may be used in lieu of butter.

Soy bean milk (Mull-soy or made by our soy bean milk formula).[15]

Soy bean or sesame oil (used as noted above).

Sugar, beet or cane, may be taken in water or in mate (Brazilian tea) or in ordinary tea.

Salt.

Mate.

Tea.

Until bowel activity decreases, feedings of moderate size should be given every two hours. Meat and soy bean are essential to meet the protein requirements. The carbohydrate foods, sugar and oil provide for sufficient calories to maintain the proper weight.

Thiamin and other synthetic B vitamins, synthetic A or caritol in sesame oil, synthetic C, and viosterol in sesame oil or Drisdol should be given as required. The approximate vitamin content of ingested foods may be determined by certain tables.* Hypermotility may prevent vitamin absorption, and, therefore, hypodermic administration, especially of thiamin and cevitamic acid, may become necessary in severe cases.

The diet should be continued for three to four weeks. Even after improvement has occurred it may be continued provided nutrition and weight are protected adequately. When improvement is unquestioned, other foods from the elimination diets may be added, one or two at a time, every seven to 14 days as follows: beef, bacon, rice, corn, spinach, asparagus, string beans, pears, peach, apricot and grapefruit. (Fruits may be tried early.) Uncooked vegetables and fruits should be added with caution. Foods commonly productive of allergy such as wheat, milk, eggs, fish, orange, apple, banana, berries, the cabbage group, honey and nuts should be given only after marked or complete relief has persisted for several weeks or months.

* Most of the recent tables may be obtained from Lela E. Booker, United States Department of Agriculture, Bureau of Home Economics, Washington, D. C.

The necessity of partial or complete exclusion of allergenic foods gradually can be determined by such diet trial. A more detailed discussion of the use and development of the elimination diet is contained in our recent manual.[15]

If the original diet has brought about no relief in three or four weeks and food allergy is definitely suspected, other elimination diets may be used for two or three months before food allergy is discarded as a possible cause. It is always possible that colonic allergy to foods in the prescribed elimination diet, or in fact to any food, may exist. Nutrition and weight at all times must be protected.

Chronic allergy, especially to foods, produces changes in cellular structure and function, recovery from which requires long freedom from the causative allergens. Thus, if the symptoms of ulcerative colitis are definitely disappearing, it is a good plan to eliminate those foods which are suspected of possible allergy for weeks provided that satisfactory weight and nutrition are maintained. Anxiety to test out suspected or additional foods may retard or obscure progress which would be continuous with the initial or a slightly enlarged diet.

Importance of Ruling Out Other Causes of Diarrhea

All causes of dysentery or diarrhea must be ruled out by thorough physical examination and indicated laboratory tests before a diagnosis of idiopathic or chronic ulcerative colitis can be made. Bacillary, amebic, and parasitical agents, intestinal tuberculosis, or malignancy, acute bacterial or virus infections, and achylia are chief among the less common causes of diarrhea and dysentery.

Cases Suitable for Allergic Study and Control

(1) Patients with fulminating ulcerative colitis should be given the elimination diet. Such diet trial is justified especially since in these cases surgical operation is associated with high mortality. Antidiarrheal medicaments, such as codeine, tincture of opium, bismuth or proteo-tannates, may be used if improvement does not result from these dietary measures in a few days. Codeine or tincture of opium should be discontinued as soon as even slight relief is obtained. It is generally conceded that colonic irrigation with so-called intestinal antiseptics is of no value. Maintenance of weight already has been emphasized. If the diet is effective, the symptoms gradually disappear in one to three weeks, and drugs become unnecessary.

(2) The elimination diets should be tried in early mild cases and in chronic cases, especially if septicemia or threatening perforation is absent. The possibility of benefit from such diet is increased when fever is absent or slight and intermittent, when proctoscopic examination reveals only erythema and granulation or scattered or superficial mucosal ulcerations, and when the blood count and sedimentation rate do not indicate much infection. If food allergy and secondary infection are possible factors in cer-

tain chronic cases, the use of elimination diets together with one of the sulfonamide drugs may be of special benefit. The time necessary for the trial diet and the subsequent addition of food has already been discussed. In these cases avitaminosis, anemia, and hypoproteinemia require proper therapy. Donald and Brown [16] recently have emphasized the importance of adequate protein and vitamin intake, especially vitamin C, until fruits and vegetables are well tolerated. Thiamin by mouth and hypodermically and liver extract parenterally as suggested by Cheney [13] may be given. Shiffer and Ferguson,[17] however, have failed to benefit cases of chronic ulcerative colitis with such therapy. Iron by mouth and blood or serum transfusions may be indicated.

(3) Because of the advisability of considering food allergy as a possible cause of non-seasonal chronic ulcerative colitis, the elimination diets should also be tried for three to six weeks in the most severe cases. In these cases weight maintenance and proper attention to avitaminosis, anemia, and hypoproteinemia are imperative. The indications for surgery, as discussed by Cave [18] and Jones [19] must be kept in mind. Although allergy may have been the initial and primary cause of the colitis, the secondary bacterial invasion with resultant cellulitis, the danger of septicemia, and of perforation of ulcerated areas may be such that the control of the allergy itself could exert no influence on the infection or pathologic condition in the colon.[20] If surgical treatment seems to be required for ultimate relief, it should be carried out before an emergency arises. The elimination diet or therapy for possible bacterial or inhalant allergy may be desirable during the preoperative and postoperative periods, if the symptoms and the physical condition of the patient are obviously improved thereby. On the other hand, the elimination diet may not be required postoperatively, even if colonic allergy has been the original cause, since the sensitized tissues are either removed through final colectomy or are prevented from contact with the allergenic foods through ileostomy. Indeed, if allergy is the primary cause of ulcerative colitis, surgery offers the possibility to remove the shock tissues themselves—an accomplishment impossible in nasal, bronchial or cutaneous allergy.

Discussion

By use of the elimination diets, complete relief of symptoms was obtained in seven of the 14 cases. The relief in Cases 2, 4 and 10 probably would have been greater if coöperation had been complete. The seasonal history did not indicate diet trial in Case 11. In six of the controlled cases specific foods reproduced diarrhea. Because of the severity of the disease in Case 3, because of the patient's complete relief, his gain of 44 pounds, and his continued ability to work in a steel foundry for three years without illness, no attempt has been made to determine the rôle of wheat and milk up to the present time. However, a piece of cake had brought on diarrhea in two hours. The small amounts of wheat, milk and egg taken

CHART I

Chronic Ulcerative Colitis

Case No.	Sex	Age	Previous History			Previous Treatment								Results from Allergic Control								
							Parenteral							Improvement						Allergic History		
			Years of Disease	Severity	Fever in	Oral Vit. B	Vit. B	Liver	Sulfonamide	Arsenic Drugs	Emetine	Vaccine	Transfusion	Onset of (Weeks)	Duration of (Years)	Degree of	Weight Gain	Cooperation	Foods Incriminated	Family	Personal	Skin Reactions
1	F	35	3	2	0									2	4	4	20	4	Milk, egg, chocolate	Asthma, hives	Nasal allergy	Foods, inhalants
2	M	29	16	4	1	+		+		+	+	+		2	4	2	6	2	Milk, several fruits, and veg.	Asthma, colitis in sister	Asthma, hay fever	Inhalants
3	M	28	1/3	4	3	+	+	+	+		+		+	2	3	4	44	4	Milk?, wheat?, chocolate?	0	0	Neg.
4	M	32	5	3	1	+		+						2	2	3	18	3	Not determined	0	0	Not done
5	M	61	1/12	4	3									4 days	1 1/4	4	10	4	Milk	0	0	Neg.
6	F	31	6	3	1	+	+	+				+		4	5/6	4	−10	4	Corn, peas, peach, onion, sweet pot.	Sick headache	Nasal allergy	Neg.
7	M	22	3	2	0									3	3/4	4	15	4	Milk, wheat?	0	0	Neg.
8	M	38	6	4	3	+	+	+	+					2	1/3	4	34	4	Not determined	0	0	Not done

CHART I (*Continued*)

Case No.	Sex	Age	Previous History			Previous Treatment								Results from Allergic Control									
							Parenteral							Improvement					Foods Incriminated	Allergic History		Skin Reactions
			Years of Disease	Severity	Fever in	Oral Vit. B	Vit. B	Liver	Sulfonamide	Arsenic Drugs	Emetine	Vaccine	Transfusion	Onset of (Weeks)	Duration of (Years)	Degree of	Weight Gain	Cooperation		Family	Personal	
9	M	8½	3	3	3									1	¼	4	10	4	Not determined	0	0	Not done
10	M	25	6	3	2				+						1	3	10	3	Nuts, berries, cabbage, sweet pot., milk	Hay fever, sick headache	Hives	Not done
11	F	43	9 Falls only	3	0							+		Pollen therapy for 1 year with complete relief						Unknown	Sick headache, hay fever	Neg.
12	F	34	¾	4	4	+	+	+	+	+	+	+	+	2	0	Death from perforation of ulcerated sigmoid						Not done
13	M	20	6	4	3	+	+	+	+	+		+		None	0	None	−15	4				Neg.
														Ileostomy—later colectomy with gain of 60 lbs.								
14	M	50	4½	3	1									2	?	1	0	4		0	Sick headache	Not done
														Still under observation								
15	M	30	5	3	2	+		+	+			+		None	Former ileostomy Recent colectomy				Eczema, nasal allergy	Hives		Not done

Degree of severity, fever, improvement and coöperation on basis of 4. 0 = None. 4 = Maximum.

occasionally by the patient in Case 4 may account for the continuance of three to four soft bowel movements a day. His gain of 18 pounds and the return of normal strength and energy indicate that he was satisfactorily controlled. Because of the chronicity of the disease and the complete involvement of the colon as shown by roentgen-ray, as well as the excellent recovery, the effect of milk and wheat in Case 6 has not yet been determined. Loss of weight at first was possibly caused by influenza, by failure to take enough calories in the diet, and by early resumption of activities. Because of the excellent results in Cases 8 and 9, the effects of common allergenic foods have not been tested. The relief by the elimination of specific foods in Case 10 was the result of diet trial elsewhere.

If symptoms return with the ingestion of specific foods, food allergy probably is the cause. Milk heads the list of allergenic foods. However, as indicated in the chart, all other foods must be suspected. Various allergists have reported the negative skin reactions to allergenic foods, especially when chronic or delayed symptoms are present. Because of the fallibility of the skin test, we have advocated certain standardized elimination diets [15] for the study of possible food allergy. In chronic ulcerative colitis Mackie [11] has used such diets to determine allergenic foods, and we have used our modified fruit-free and cereal-free elimination diet as suggested in this article. As indicated in chart 1, skin testing has not been of any definite or uniform help in our diet trial. However, possible allergy has been suggested by disagreements with or distastes for specific foods, especially for milk, as obtained from the diet history (see Case 3).

When good results were obtained, relief was evident in from one to four weeks, and in the acute fulminating Case 5 it was definite in four days after the diet was initiated. In some cases maximum improvement required several months, probably because of the chronic tissue changes and the varying degree of secondary infection. Excellent results were obtained in six patients who failed to give a family or personal history of allergy. If allergy is a major cause in these patients, we must conclude that the colon is the only evident shock organ. The negative family history may be owing to lack of complete information.

In view of the benefit of the B vitamins, especially of thiamin and liver therapy as reported by Cheney,[13] the possible effect of such treatment on these patients must be considered. In five of the most severe cases, no response to such treatment had been noted before the diet trial was begun. Of interest is the recent report of Shiffer and Ferguson [17] that thiamin and liver injections were of no benefit in this disease. In Cases 1, 5, 7, 9 and 10 such therapy had not been used although good results were obtained with the elimination diet within three weeks. As previously stated, in all patients with chronic ulcerative colitis avitaminosis must be combated with proper therapy. Likewise anemia and hypoproteinemia must be treated specifically. This had been done along with diet trial when indicated in our patients. However, the good results, especially in those patients who

had received previous vitamin B and liver therapy, and in the patients in Cases 1 and 5 who received no additional vitamin therapy during the first month of dietary therapy, apparently were derived from the elimination diet.

Sulfonamide drugs were given by mouth while elimination diets were being used in Cases 3, 8 and 9. In Case 3 neoprontosil was administered for two weeks in two courses during the first six months after relief had occurred. The reduction from five or six to two to four soft stools indicated the possible alleviation of a mucosal infection. Proctoscopic examination showed that the scattered superficial ulcerations and a moderately purulent secretion also had decreased. This patient had received metaphen every few days by vein for two weeks before the diet was instituted. This medication was continued for three weeks thereafter. In view of this patient's complete recovery in the last three years and the results in our other cases, it is my opinion that relief did not depend on the metaphen. Sulfaguanidine was given in Case 8 for two weeks about two weeks after trial diet had been instituted. Failure to respond to previous sulfanilamide and sulfaguanidine therapy, however, and the definite relief in two weeks after diet trial was started indicate the probability that food allergy was the cause of the colitis. In Case 9 one or two formed stools per day occurred during the first two weeks of diet trial. However, the continuation of fever indicated that probably the infection in the bowel had persisted. For this reason sulfaguanidine was given for one and one-half months. Bargen's vaccine and a stock respiratory vaccine also were administered in the hope of increasing resistance to bowel organisms, although the fever disappeared in the first few days of such drug therapy and normal bowel movements had occurred before it was begun.

The failure of the sulfonamide drugs to produce definite benefits in Cases 3, 8 and 10 before diet trial was used and their failure in Cases 12, 13 and 15 in which septic temperatures were present and failure to respond to diet trial had occurred also indicate that in this disease they are not of the value anticipated.

Summary

1. Allergic colitis, especially when caused by foods, results in diarrhea, mucus, bleeding, tenesmus, pain and cramping. This localized allergy produces inflammation, mucoid secretion, increased capillary permeability or smooth muscle spasm in varying degrees.

2. Chronic ulcerative colitis may be caused by severe allergic reactivity in the colonic mucosa similar to that responsible for atopic dermatitis. Ulcerations may arise from superimposed secondary infection from various bowel bacteria or possibly from lesions similar to canker sores in the mouth. Resultant ulcerations, mucosal denudation, fibrosis, scar tissue formation, and bowel perforation vary according to the degrees of resistance to infection.

3. Fruit-free elimination diets are recommended for the study of possible food allergy in these cases.

4. These diets are indicated especially in the acute fulminating and mild chronic cases. They may also be used in severe intractable cases as long as surgical treatment is not definitely indicated.

5. With such diets the maintenance of weight and the control of avitaminosis, hypoproteinemia, and anemia are necessary. The use of the sulfanilamide drugs may benefit associated secondary infection.

6. That chronic ulcerative colitis may be due to inhalant or bacterial allergy must also be considered.

7. In intractable cases the study of possible allergy should not delay surgical treatment when it is obviously indicated.

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INTERCAPILLARY GLOMERULOSCLEROSIS *

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This syndrome of diabetes, hypertension and nephrosis was first described in 1936 by Kimmelstiel and Wilson.[3] They stressed the unusual and consistent pathological changes found in the kidneys, namely, degenerative changes in the walls of the capillaries, arterioles and vasa afferentia of the glomerular tufts. These authors reported eight cases with clinical and pathological findings. More recently Anson [2] reported six similar cases. Newburger and Peters,[1] in 1939, reviewed the two former papers and presented autopsy protocols of four cases and five cases in which the pathological renal lesions were suspected. A comprehensive analysis of the clinical, laboratory and pathological findings was included. Derow, Altschule and Schlesinger [4] also published a detailed clinical and pathological report of one case. In the Cabot [5] case reports of the Massachusetts General Hospital of July, 1940, appeared a rather unusual clinical and pathological report of a 22 year old girl who had had known diabetes for two and one-half years. This is the youngest case reported of this syndrome. Kimmelstiel and Wilson concluded that diabetes mellitus, hypertension, albuminuria, retinal vascular changes, a more or less well developed nephrotic syndrome, and impairment, in a varying degree, of renal function occurred in most of the cases in which the characteristic renal lesions were found. Most of the patients were elderly. Edema of a nephrotic type rather than that of renal or cardiac failure was a persistent finding. There was a constant marked albuminuria with or without nitrogen retention, indicating renal rather than cardiac involvement.

Newburger and Peters [1] listed the following clinical characteristics:

(1) All patients were over 40 years of age (except one that was 35) at the time of the onset of the diabetes or albuminuria or both.

(2) Fourteen of the 21 cases were women.

(3) Diabetes mellitus, usually mild in type, was present in all cases.

(4) Albuminuria, usually heavy, was present in a varying degree in all cases, especially before death occurred.

(5) Retinal arteriosclerosis was present in all cases; in addition papilledema, fresh hemorrhages, and exudates characteristic of the malignant phase of hypertension were present in five cases.

(6) Hypertension occurred in varying periods in all cases.

(7) Edema of some degree was present in the entire group, varying inversely to the level of the serum albumin, which in turn depended on the severity of the albuminuria and on the protein intake.

* Received for publication March 3, 1941.

(8) Heart failure when present was chiefly left sided.

(9) Low specific gravity of the urine, azotemia, and hypochromic anemia were commonly found.

Two similar cases with autopsy reports are being presented which satisfy the criteria for this symptom complex. Both of these cases gave clinical evidence of extensive degenerative vascular changes.

Case Reports

Case 1. A white woman, aged 59, was first seen in December 1937, at which time she was known to have had diabetes for four months, with suggestive symptoms for several years. The diabetes was under satisfactory control with insulin and diet. Her chief complaint was pain of a neuritic type in her extremities, which had been present in varying degree for two years.

The past history was irrelevant except for recurrent attacks of headache up to the menopause. She had been nauseated a great deal the past few years. In her young adulthood she had had a post-diphtheritic polyneuritis.

Physical examination revealed a rather poorly nourished white woman who appeared slightly older than her years, constantly complaining and obviously suffering from acute pain in her legs but able to walk. The relevant findings were a flushed, florid facies with a puffy appearance, bilateral clouding of the lenses of both eyes, marked arteriovenous nicking, and a silver wire appearance of the arteries of the fundi. The left border of the heart was 11 cm. from the midsternal line in the sixth interspace. The blood pressure was 180 mm. Hg systolic and 110 mm. diastolic. The liver was palpated one finger's breadth below the right costal margin. The patellar and Achilles reflexes were not elicited even with reënforcement. However, the other reflexes were intact, and there were no sensory disturbances.

Laboratory reports at this time showed mild hypochromic anemia, normal blood serology, and a urine with a specific gravity of 1.012, albuminuria +++ (on a basis of 1–4), and a slight reduction of Benedict's solution. The blood sugar was 150 mg. per 100 c.c. three hours after breakfast.

The neuritic pains gradually responded to large doses of vitamin B complex by mouth and massive doses of thiamin hydrochloride hypodermically. Anorexia with intermittent nausea and vomiting was persistent. Increasingly large amounts of insulin were required. At times she appeared slightly edematous especially about the face. Her systolic blood pressure gradually rose to over 200 mm. of Hg with a diastolic pressure of over 110 mm. In July 1938, she was hospitalized because of intractable nausea and vomiting for which no definite cause was found. At this time the blood urea nitrogen was 22.9 mg. per cent, nonprotein nitrogen 50 mg. per cent, CO_2 combining power 55 vol. per cent, blood sugar 155 mg. per cent (fasting), and the bromsulphalein liver function test showed no dye retention. There was a persistent albuminuria and a low urinary specific gravity. Hemoglobin was 94 per cent. Spinal fluid was normal.

She was then quite well except for slight neuritic pains, general irritability, and occasional anorexia and nausea. She gained in insulin tolerance but her hypertensive level persisted.

In September 1939, her blood pressure was 240 mm. Hg systolic and 120 mm. diastolic, and she felt quite well aside from anorexia. She was started on potassium thiocyanate 1 gm. daily. The vitamin B therapy was continued together with 0.045 gram of phenobarbital daily. Several weeks after this it was noticed that although she was eating very little her weight was gradually increasing. In October 1939, her blood pressure was 160 mm. Hg systolic and 110 mm. diastolic. During the first

week in November, the patient complained of a rapid gain in weight. There was edema of her ankles, she was slightly dyspneic, and her pulse rate was elevated so that digitalization was started. Weakness rapidly developed and nausea was present. Her temperature was 100.6° F., and pulse rate 94 per minute. She was generally edematous, especially in the face, with pitting edema of the extremities. She was again hospitalized on November 14, 1939, and became steadily worse. Edema persisted and later slight ascites developed. She had constant nausea and vomited nearly all ingested food. There was a low grade fever for several days after which it spiked to 102° F. daily. She developed fluid in the right pleural cavity which was confirmed by fluoroscopy. A straw-colored sterile fluid was aspirated on two occasions.

She gradually developed a secondary anemia but her leukocyte count remained around 15,000 per cu. mm. with 30 to 40 per cent non-segmented polymorphonuclear cells. Heavy albuminuria was constantly present being as high as 3.5 per cent by volume with a specific gravity about 1.010. The blood urea nitrogen was 11 mg. per 100 c.c., the non-protein nitrogen 30 mg. per 100 c.c., the carbon dioxide combining power 67 volumes per cent, and the blood chlorides 313 and 370 mg. per 100 c.c. on two occasions. Blood sugar determinations were constantly below 150 mg. per 100 c.c. With fluid formation in the right pleural cavity, dyspnea with the slightest exertion occurred. She developed a cough two days prior to her death, with some bloody sputum on several occasions.

The patient did not respond to treatment which consisted of intravenous infusions of sodium chloride and glucose solution, a blood transfusion, various diuretics, including mercurials, digitalization and other supportive measures. She died on December 2, 1939.

Pathological Report: The usual ventral midline incision revealed rather edematous, pale abdominal fat.

There were approximately 75 c.c. of clear fluid in the right pleural cavity and 275 c.c. of turbid fluid in the left pleural cavity. The right lung was extremely congested throughout. The left lung was voluminous and deep red. There was a large hemorrhagic infarct in the upper lobe extending into the apex, having a base of 5 cm. A large hemorrhagic infarct involved almost the entire left lower lobe, and the pleural surface was covered with a fibrinopurulent exudate. The cut surfaces showed a diffuse pneumonitis in the remaining lung tissue.

The heart was enlarged, the walls hypertrophied and somewhat dilated. The right auricle showed a marked dilatation and contained a mural thrombus in the auricular appendage. The wall of the right ventricle was hypertrophied. There was a moderate amount of atheromatous deposits in the aorta which were progressive in degree distally. Approximately 4 cm. above the junction of iliac arteries there was a small dissecting aneurysm of the posterior wall of the aorta, which extended only for a distance of approximately 3 cm. The entire vascular tree was sclerotic and presented numerous atheromatous plaques in the larger vessels.

The liver was enlarged and showed chronic passive congestion.

The pancreas showed interlobular fibrosis. The spleen was enlarged and markedly congested.

Both kidneys were enlarged and firm, and the capsules were moderately adherent. They showed a moderate amount of nephrosclerosis, and the pelvis showed some increase in fat. The ureters and bladder showed no definite abnormalities. Microscopic report (see under Case 2).

*Case 2.** A white male was referred to Dr. Hobart Rogers for treatment of diabetes mellitus in April 1937, a condition the patient had been aware of for six months. He had always been obese, his average weight being 240 pounds, up until five years previously when he gradually began to lose weight, the reduction being

* We are indebted to Dr. Hobart Rogers for the data on this case.

more rapid the past year. During the past three years he had had periods of polydypsia and polyuria lasting for a month or so. However, these symptoms were never marked. There had been generalized pruritus during the past six months.

He complained of pain and stiffness in the right shoulder. He also suffered from angina of effort.

His past history was irrelevant. The family history revealed no pertinent information except that there was one brother with diabetes mellitus.

Physical examination on April 5, 1937, revealed an obese white male weighing 187 pounds, 66¾ inches in height, with a temperature of 97.4° F., pulse of 70 per minute, and a blood pressure of 180 mm. Hg systolic and 85 mm. diastolic. The mouth was edentulous, the lungs were clear, and the left border of the heart was one inch outside the midclavicular line in the fifth left interspace. There was a blowing systolic murmur of moderate intensity heard over the apex and over the precordium and somewhat higher pitched at the aortic area. The reflexes were generally diminished. The dorsalis pedis pulsations were barely perceptible.

Laboratory data at this time showed a negative Kline test, heavy glycosuria (other date was not recorded), blood sugar of 299 mg. per 100 c.c.

Fluoroscopy of the chest showed enlargement of the left ventricle of the heart and arteriosclerotic changes in the aorta. The electrocardiogram showed maximum normal A–V conduction-line, left axis deviation and low amplitude of the T-waves.

The patient was placed on a diabetic régime with a low caloric diet and insulin. He rapidly gained in insulin tolerance so that by July his dosage had been reduced from 66 to 30 units daily. The anginal pain was more frequent when the blood sugar was reduced to a normal level. The shoulder discomfort responded to symptomatic treatment. By August 1938, the insulin requirement had dropped to 8 to 12 units of protamine zinc insulin daily. Later the patient had less anginal pain with a reduction of his diet without insulin. His weight was 208 pounds. He complained at various times of nausea and pain across his lower abdomen. In March of 1939 the patient developed dyspnea on exertion, ankle edema and ascites. He was digitalized and given mercurial diuretics with good relief. At this time his weight was about 190 pounds.

In November 1939, the patient had a typical attack of coronary occlusion which was verified by an electrocardiogram which also suggested increased myocardial damage. The patient had edema and spells of weakness and breathlessness. He responded fairly well following this episode, but after January 1940, the edema of the legs and sacrum was more marked, and there was heavy albuminuria with hyaline casts in the urine.

At this time the blood urea was 21 mg. per 100 c.c. and blood sugar 190 mg. per cent. The blood pressure was 160 mm. Hg systolic and 100 mm. diastolic. He became confused and irritable, amblyopia developed, and there was increased peripheral edema. Liver enlargement became noticeable but mercurial diuretics controlled the edema fairly well. At this time a diagnosis of intercapillary glomerulosclerosis was made. In March 1940, there was a severe gastrointestinal hemorrhage, thought to be due to esophageal varices, secondary to cirrhosis of the liver. After this the patient declined rapidly and died suddenly on March 9, 1940.

Pathological Report: The abdominal cavity contained about a liter of lightly bile stained fluid. On the lesser curvature of the stomach about two inches proximal to the pylorus there was a chronic ulcer 2 cm. in diameter with a smooth base and indurated edges. Sclerotic vessels could be seen on the peritoneal side of the ulcer base.

The liver was large and firm with a sharp edge which was cut with increased resistance. The gall-bladder contained a solitary stone 2 cm. in diameter.

The kidneys were about normal in size and the right showed two small scars. The capsules stripped fairly easily. Section of the kidneys experienced increased resistance. The cortex was thin and fibrotic.

The pleural cavities were dry and the lungs crepitant throughout. Subpericardial fibrosis was present about the pericardium. There was evidence of two old myocardial infarcts near the apex. The surfaces made by cutting revealed these areas to be thin and soft. Subendocardial fibrosis was also evident. The orifices of the coronary arteries were slightly constricted and the coronary arteries showed atherosclerosis throughout their courses.

Microscopic Report: The microscopic sections taken from the kidneys of both cases showed various stages of sclerosis of the glomeruli, ranging from early fibroblastic proliferation to hyalinization. The earlier and intermediary stages showed a relatively well preserved capillary system within the glomeruli with fibrosis between the tufts (intercapillary fibrosis). Differential stains showed the capillaries in these stages to be intact with fibrous proliferation in the intercapillary spaces.

Discussion

As Newburger and Peters have stated, the pathogenesis of this disease seems to depend upon the severe and extensive arterial and arteriolar degeneration associated with diabetes mellitus, hypertension, and renal damage. The two cases presented gave evidence of far advanced vascular degeneration with retinal artery sclerosis, hypertension and persistent albuminuria.

Only with the earlier recognition of this syndrome may it be possible to obtain more information concerning the contributing and causative factors and make more successful methods of therapy available. Even then there is no assurance that the progression of the pathological processes can be retarded. Both of the cases presented were recognized in the terminal stages. Studying the pathogenesis in retrospect, it is hard to determine what other procedures, methods or drugs might have been more efficacious.

Summary

Two additional cases of intercapillary glomerulosclerosis have been presented.

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TRANSITORY PULMONARY INFILTRATIONS MISTAKEN FOR TUBERCULOSIS, WITH A REPORT OF FIVE CASES *

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FOR some time the chest roentgenogram has been the most valuable diagnostic measure in the recognition of pulmonary tuberculosis. It has been shown repeatedly that physical examination of the chest as the only procedure in the diagnosis of pulmonary diseases is entirely inadequate. Spellman [1] gives an illuminating exposition of this fact in a recent article relating the experience of attempting, by physical examination, to detect pulmonary tuberculosis in army recruits in 1917–1918. It is not the purpose of the present authors, therefore, to minimize the efficacy of the roentgenogram in the diagnosis of pulmonary tuberculosis.

Five patients are presented, whose chest roentgenograms showed densities strikingly simulating tuberculous infiltrations which, however, proved to be non-tuberculous. In each of the five cases a diagnosis of pulmonary tuberculosis was originally made by one or more competent roentgenologists or phthisiologists. From the data available at the time the five patients were first observed the diagnoses were not questioned by the present writers. However, doubt was cast on the original diagnoses when examination of the sputum and aspirated gastric contents with direct smears, concentrations, cultures or guinea pig inoculations failed to disclose the presence of tubercle bacilli. Subsequent serial roentgenograms confirmed the non-tuberculous etiology of the pulmonary infiltrations.

To venture a diagnosis on a single roentgenogram of a patient's chest frequently leads to error. The demonstration of tubercle bacilli in the sputum should be the criterion in the final diagnosis of broncho-pulmonary tuberculosis. Probably in almost 100 per cent of the cases of active pulmonary tuberculosis tubercle bacilli can be found, if sufficiently thorough searches are made. If tubercle bacilli are absent, it is a safe rule to consider the pulmonary pathologic changes non-tuberculous in nature and to proceed with the various special examinations, such as bronchoscopy, etc., in order to arrive at a diagnosis.

With the universal use of artificial pneumothorax therapy in pulmonary tuberculosis the above remarks are pertinent. The value of this form of therapy in pulmonary tuberculosis is established beyond any doubt, but it may be unnecessary or even harmful in other pulmonary diseases. In the zeal for rehabilitating the tuberculous individual patient it is wise to establish first whether the patient has tuberculosis.

* Received for publication November 26, 1940.
From the Workmen's Circle Sanatorium, Liberty, New York.

Case Reports

Case 1. S. S., male, aged 51 years, was admitted to the Workmen's Circle Sanatorium on May 24, 1939. For the past 15 years he had been the owner of a confectionery store. Prior to that time he had worked as a tailor. He did not recall any childhood illnesses. He had had pneumonia 18 years previously and a tonsillectomy 15 years previously. At intervals, for many years, the patient had had attacks of moderate dyspnea which he attributed to asthma. These episodes did not inconveni-

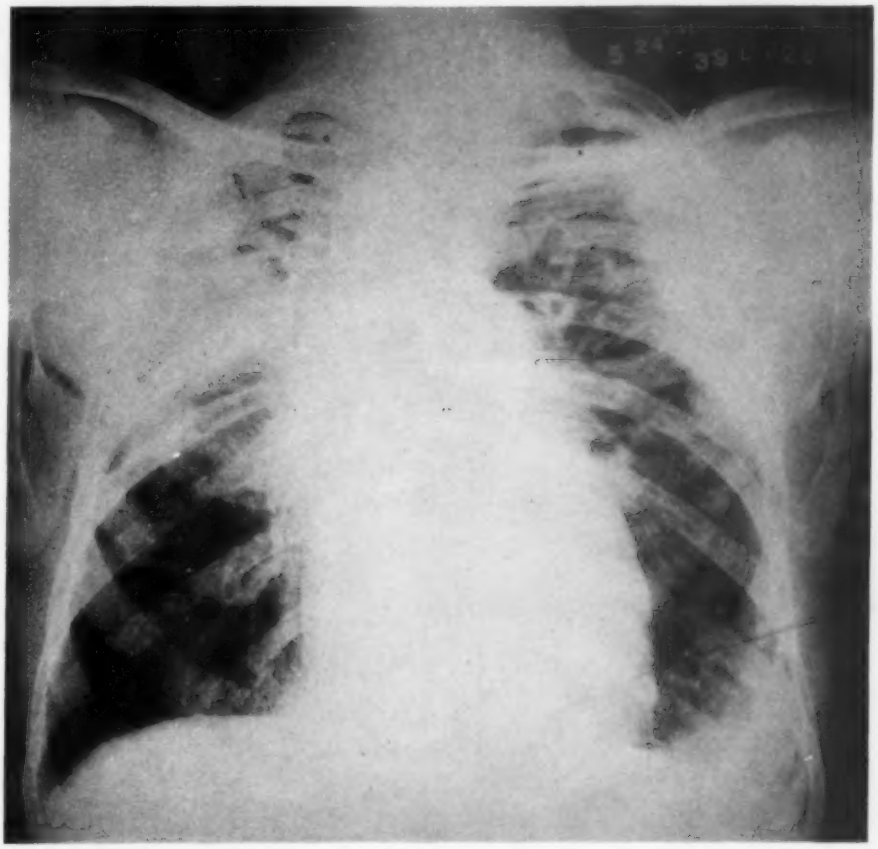

Fig. 1. (Case 1.) Roentgenogram taken May 24, 1939. Dense infiltrations throughout the left lung and the upper two thirds of the right lung. The cardiac silhouette is moderately enlarged particularly to the left.

ence him very much and he did nothing about them. The patient's story of the onset and symptoms of his present illness was also rather vague and indefinite. About six weeks prior to his admission to the Sanatorium he began to feel weak, lose appetite and weight, and he began to have pain over the left side of his chest. He visited a physician who referred him for a roentgenogram of his chest. A diagnosis of pulmonary tuberculosis was made, and he was advised to enter a sanatorium.

The noteworthy findings on the patient's admission to the sanatorium were poor nutrition, pale, dry skin, pale nasal mucosa, enlarged right tonsil, and slight congestion of vocal cords. On physical examination the heart did not show any enlargement;

rate was 108 per minute; rhythm was regular; sounds were of good quality; no murmurs were heard; the second pulmonic sound was accentuated. Blood pressure was 90 mm. Hg systolic and 62 mm. diastolic. Physical examination of the lungs showed dullness, bronchovesicular breathing, and medium moist râles over the right upper lobe anteriorly and posteriorly. Sibilant and sonorous râles were heard over the entire left lung anteriorly and posteriorly with bronchovesicular breathing over the

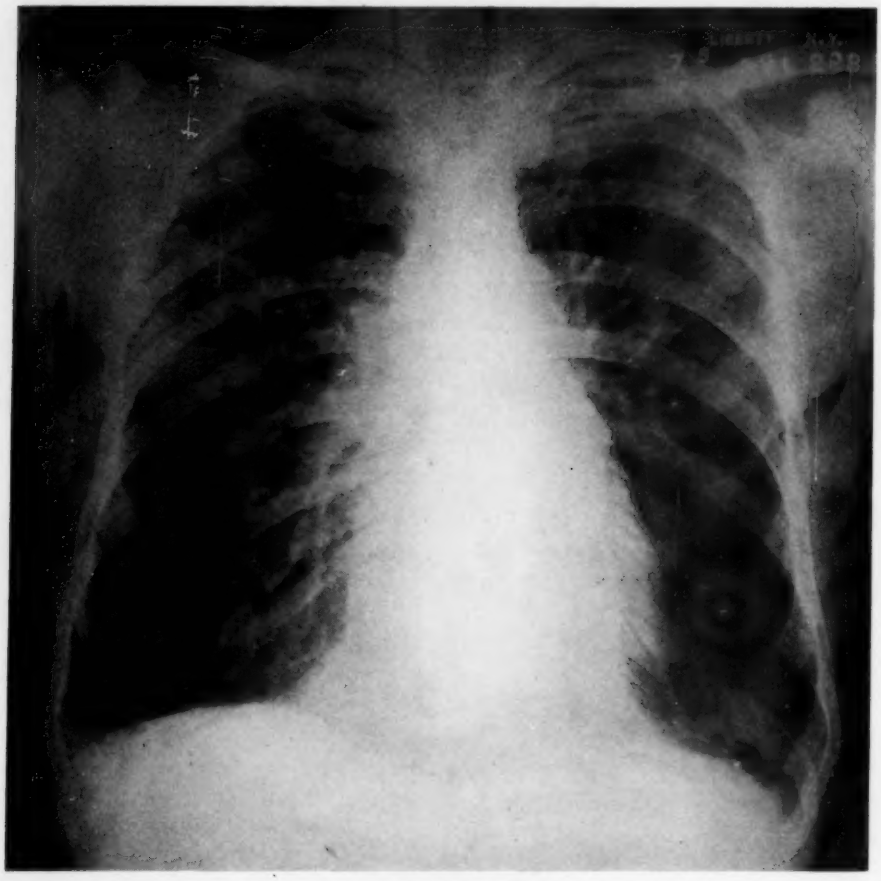

FIG. 2. (Case 1.) Roentgenogram taken July 5, 1939. Complete clearing of the right lung field; slight infiltration left upper lobe. The cardiac silhouette remains enlarged with straightening of the left border.

upper lobe and dullness over the base. There was cyanosis of the finger nails and feet. Both legs showed marked varicosities.

Laboratory Data. May 25, 1939. Urinalysis was negative. The blood count showed: hemoglobin, 86 per cent; red blood cells, 4,460,000 per cu. mm.; white blood cells, 19,300 with polymorphonuclears, 43 per cent; lymphocytes, 48 per cent and eosinophiles, 9 per cent. Erythrocyte sedimentation rate, 54 mm. in one hour; Kahn reaction negative; non-protein nitrogen, 28.5 mg. in 100 c.c. of blood. On August 14, 1939, the hemoglobin was 92 per cent; red blood cells, 4,740,000; white blood cells, 17,450 with polymorphonuclears, 74 per cent; lymphocytes, 20 per cent; monocytes, 1 per cent and eosinophiles, 5 per cent. The erythrocyte sedimentation rate was 5 mm.

in one hour. Seven sputum examinations, including four of concentrated sputum, and culture did not show the presence of tubercle bacilli. Vital capacity (May 25, 1939) 1500 c.c. An electrocardiogram taken on May 24, 1939, showed an auricular and ventricular rate of 110 and right axis deviation, otherwise within normal limits. The electrocardiogram was repeated on June 19, 1939, following the administration of

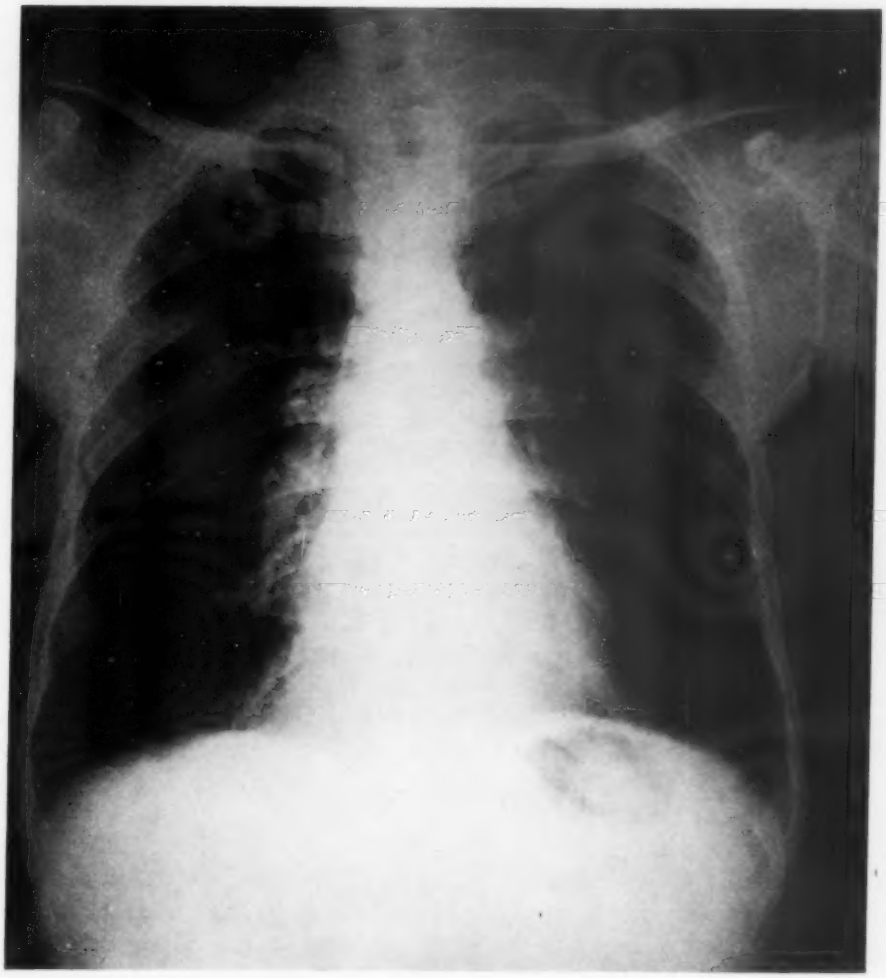

FIG. 3. (Case 1.) Roentgenogram taken September 5, 1939. Both lung fields clear. Cardiac silhouette normal in size and configuration.

digitalis, and it showed a depression of the R–T segments in Leads II and III; otherwise it showed no change from the previous electrocardiogram. Another electrocardiogram taken on August 17, 1939, showed an auricular and ventricular rate of 90, and it was otherwise unchanged from the first electrocardiogram, taken on May 25, 1939.

Roentgenograms. On May 24, 1939, a chest roentgenogram (figure 1) of this patient showed dense infiltrations throughout the left lung and upper two-thirds of the right lung. The cardiac silhouette showed moderate enlargement particularly to the

left. Fluoroscopic examination of the heart revealed slight enlargement of the left ventricle and more marked enlargement of the right ventricle. On June 13, 1939, the roentgenogram showed marked clearing of both lung fields; there was no change in size or configuration of the cardiac silhouette. On July 5, 1939, the roentgenogram (figure 2) showed complete clearing of the right lung field and remaining slight infiltration in the left upper lobe. The cardiac silhouette remained enlarged with straightening of the left border. On August 5, 1939, the chest roentgenogram was within normal limits except for evidence of emphysema. The straightening of the left border of the cardiac silhouette was not as marked as in the previous film. The last roentgenogram (figure 3), on September 5, 1939, showed no change in the lung fields from the film taken on August 5, 1939. The cardiac silhouette had returned to normal in size and configuration.

Course. On admission to the Sanatorium the patient was moderately dyspneic. There was also cyanosis of the finger nails and feet. That of the latter might have been due, in part, to the varicosities of both legs. Digitalis was administered, but was discontinued owing to its apparent lack of effect on the heart rate and the dyspnea. After about six weeks' stay in the Sanatorium the dyspnea and cyanosis began to subside, and prior to discharge the patient had no greater amount of dyspnea than would be expected in any individual with moderate emphysema. The cyanosis had completely disappeared. The patient ran an afebrile course and gained 13 pounds in weight. During his entire stay in the sanatorium the amount of cough and expectoration was negligible. The patient was discharged on September 17, 1939, and he returned to his usual activities.

Comment. In this case the original diagnosis of pulmonary tuberculosis was based essentially on the roentgen findings. Subsequent observation proved that the diagnosis was incorrect. In attempting to arrive at a correct diagnosis left-sided heart failure with one or a combination of the following common complications was considered; namely, pulmonary engorgement, pulmonary edema, pulmonary infarction and bronchopneumonia. However, the visualization, on fluoroscopic examination, of relatively more pronounced enlargement of the right ventricle, the accentuation of the second pulmonic sound, and the evidence of right axis deviation on the electrocardiogram, all pointed essentially to a right ventricular strain. Evidence was also lacking of the presence of hypertension, coronary arteriosclerosis, and mitral or aortic valvular disease, which tended to confirm the impression that the clinical picture was one of cor pulmonale. Apparently, the pulmonary manifestations were not the result of left ventricular insufficiency but rather due to the fact that the pathologic changes in the lungs produced increased resistance in the pulmonary circuit, with consequent hypertension in the pulmonary artery, followed by dilatation and possible hypertrophy of the right ventricle. The nature of the pulmonary infiltrations will be discussed later.

Case 2. F. K., female, aged 26 years, a school teacher, was admitted to the Workmen's Circle Sanatorium on November 2, 1937, during the fourth month of her first pregnancy. In childhood she had whooping cough, measles, chicken pox and influenza. Two weeks prior to admission she was taken acutely ill with fever and cough productive of about two drams of yellowish sputum in 24 hours. She was seen by two phthisiologists who diagnosed pulmonary tuberculosis and advised immediate admission to a sanatorium and induction of artificial pneumothorax. Interruption of the pregnancy was considered but not carried out.

The noteworthy physical findings on the patient's admission to the sanatorium were mild anemia of finger nails and eyelids, obvious symmetrical enlargement of thyroid, palpable but not markedly enlarged submaxillary glands, slight malar flush, and moist skin. The pharynx was slightly congested, and the anterior pillars and epiglottis were injected. The heart was entirely negative. Blood pressure was 94 mm. Hg systolic and 68 mm. diastolic. The abdomen was slightly protuberant; the uterus was enlarged midway between the symphysis and umbilicus. The lungs showed

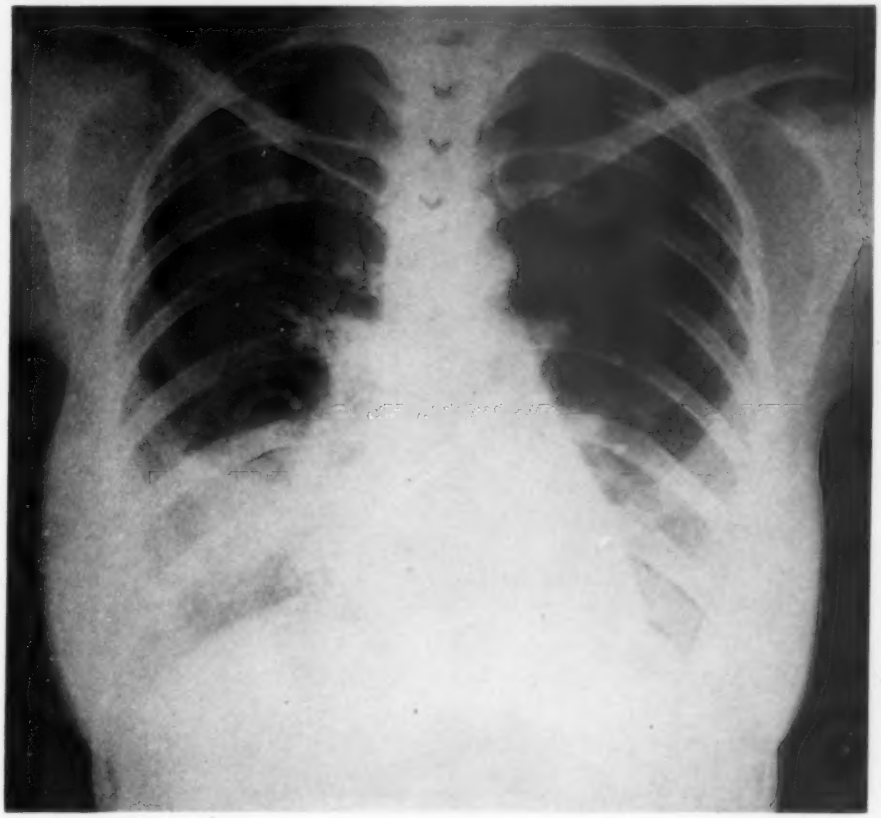

FIG. 4. (Case 2.) Roentgenogram taken October 28, 1937. Infiltration in the right infraclavicular region with bronchogenic spread to the right base.

bronchovesicular breathing over the right upper lobe anteriorly, dullness over the right upper lobe posteriorly, distant bronchial breathing, and medium moist râles from the right angle of the scapula to the base.

Laboratory Data. November 3, 1937. Urinalysis negative. The blood count showed: hemoglobin, 70 per cent; red blood cells, 4,000,000 per cu. mm.; white blood cells, 10,200 with polymorphonuclears, 73 per cent; lymphocytes, 22 per cent and monocytes, 5 per cent. Erythrocyte sedimentation rate, 59 mm. in 60 minutes. Kahn test was negative. On November 21, 1937, the blood count was as follows: hemoglobin, 68 per cent; red blood cells, 3,950,000; white blood cells, 8,000 with polymorphonuclears, 65 per cent; lymphocytes, 30 per cent; monocytes 2 per cent and

eosinophiles, 3 per cent. Erythrocyte sedimentation rate, 36 mm. in 60 minutes. Five sputum examinations, including three of concentrated sputum, and one culture did not show the presence of tubercle bacilli.

Roentgenograms. A chest roentgenogram (figure 4), taken on October 28, 1937 (prior to admission), showed infiltration in the right infraclavicular region with bronchogenic spread to the base. The left lung was negative. The roentgenogram taken on November 3, 1937, on admission to the sanatorium, showed no change from

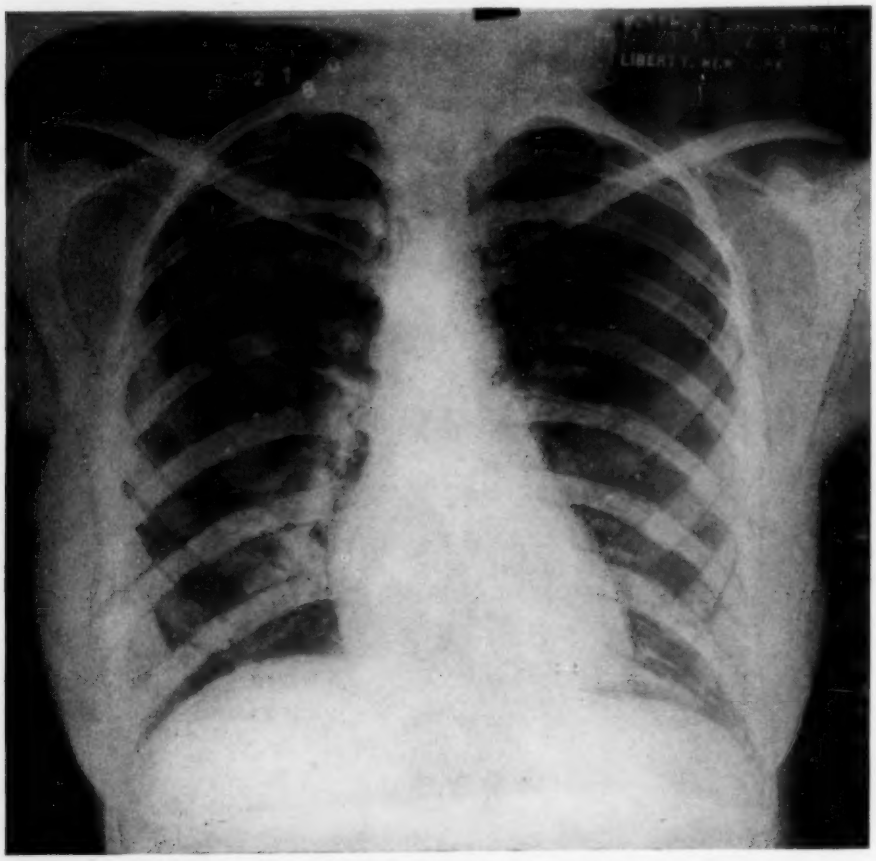

FIG. 5. (Case 2.) Roentgenogram taken November 13, 1937. Marked clearing of the right lung field.

the previous film. On November 13, 1937, a roentgenogram (figure 5) showed marked clearing of the right lung field so that only accentuation of the lung markings remained. The left lung was negative. A roentgenogram taken on November 20, 1937, showed no evidence of any abnormal changes in either lung.

Course. During the patient's stay in the sanatorium she ran an afebrile course and gained two pounds in weight. The productive cough subsided, and prior to discharge, disappeared entirely. She was discharged from the sanatorium on November 21, 1937. At term she had an uneventful delivery. To date she has shown no evidence of having any active pulmonary tuberculosis.

Comment. This is another illustration of a mistaken diagnosis of tuberculosis based on the roentgenogram. The original diagnosis was disproved by serial roentgenograms, which showed the rapidity with which resolution of the pulmonary infiltration took place, and the failure to find tubercle bacilli in the sputum. This patient had a non-tuberculous bronchopneumonia resembling in many respects the type described by Reimann and Havens.[2] The causative agent is thought to be a filtrable virus. Unfortunately, typing of the sputum was omitted at the onset of the illness prior to admission to the sanatorium.

Case 3. E. P., male, aged 23 years, clerical worker, was seen by one of the present writers (A. A. K.) on July 23, 1933. In childhood he had had measles. On July 22, 1933, the patient developed what he termed a "cold" accompanied by an unproductive cough. He felt somewhat feverish but did not take his temperature, and he did not feel sufficiently ill to go to bed. When the patient appeared for examination the

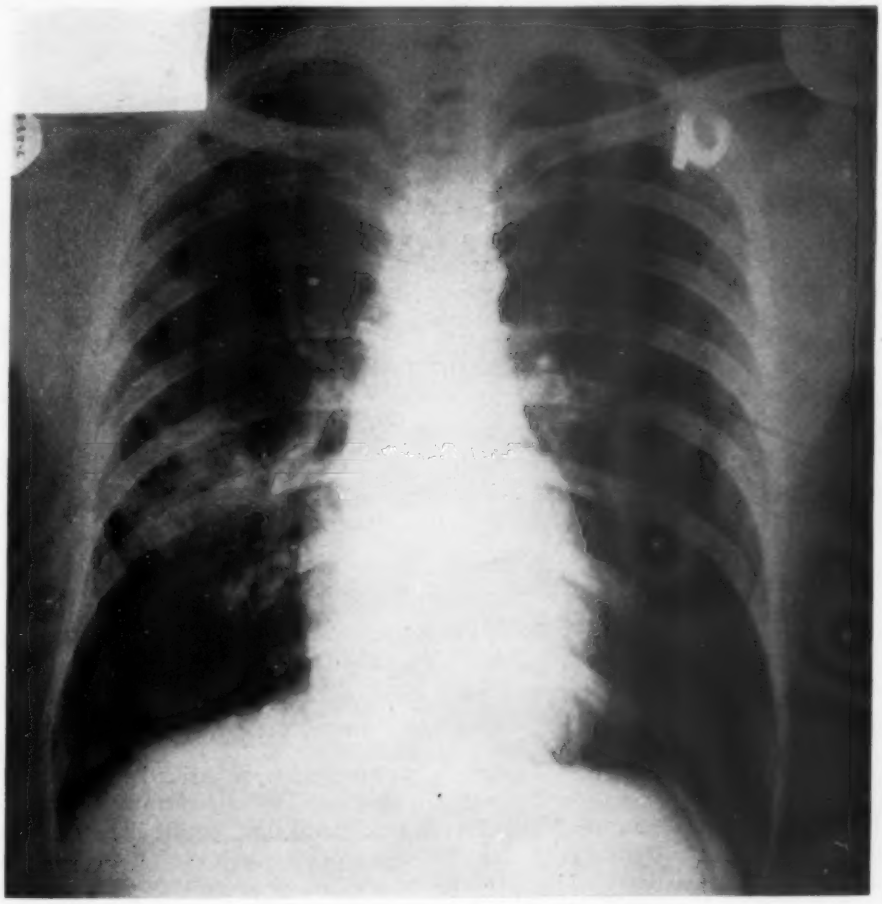

FIG. 6. (Case 3.) Roentgenogram taken July 23, 1933. Infiltration in the right lung between the fourth and fifth anterior ribs.

following day he had a temperature of 102.4° F. His only other complaint was that of cough, which had become somewhat productive of yellowish sputum.

The significant findings on examination were congestion of the pharynx and epiglottis. The lungs and heart were entirely negative, and the blood pressure was 120 mm. Hg systolic and 80 mm. diastolic. There were no other noteworthy physical findings.

Laboratory Data. July 24, 1933. Urinalysis negative. The blood count showed: hemoglobin, 90 per cent; red blood cells, 4,600,000 per cu. mm.; white blood cells, 8,700 with polymorphonuclears, 76 per cent; lymphocytes, 22 per cent; monocytes, 1 per cent and eosinophiles, 1 per cent. Erythrocyte sedimentation rate, 36 mm. in 60 minutes. Wassermann reaction was negative. Eight sputum examinations and inoculation of guinea pigs with two sputum specimens, collected on different days, did not show the presence of tubercle bacilli.

Roentgenograms. A chest roentgenogram (figure 6), taken on July 23, 1933, showed infiltration in the right lung between the fourth and fifth ribs anteriorly. The remainder of the right lung and the left lung showed accentuation of the lung markings. On July 27, 1933, the chest roentgenogram showed almost complete clearing of the infiltration in the right lung field. The accentuation of the lung markings in both lungs was still present. On August 3, 1933, the roentgenogram showed complete clearing of the infiltration in the right lung field. Some accentuation of the lung markings in both lungs was still evident. On August 10, 1933, the roentgenogram (figure 7) showed no abnormal changes.

Course. Four days after the onset of symptoms the patient's temperature returned to normal. The productive cough disappeared in a week. He was kept in bed about three weeks. After three months, when it was definitely determined that the inoculated guinea pigs did not show any evidence of tuberculous infection, the patient was allowed to return to his usual activities of life. This patient has been observed from 1933 until the present time; chest roentgenograms have been taken at least once yearly. To date there has been no evidence of any active pulmonary tuberculosis.

Comment. Following the first roentgenogram this patient's case was reviewed by a group of phthisiologists at a tuberculosis sanatorium conference. The diagnosis of pulmonary tuberculosis was not questioned and induction of an immediate pneumothorax was recommended. As in the previous case, the diagnosis was non-tuberculous bronchopneumonia probably caused by a filtrable virus. Since the episode occurred during the month of July it seemed rather remote, during the first few days of the patient's illness, to identify the clinical picture with that of epidemic influenza bronchopneumonia. The serial roentgenograms pointed to the non-tuberculous nature of the pulmonary infiltrations. The absence of tubercle bacilli confirmed that impression. It would have been of interest to have had this patient's sputum typed. Unfortunately it was not done.

Case 4. I. R., male, aged 48, a dress manufacturer, was admitted to the Workmen's Circle Sanatorium on July 15, 1940. In childhood he had had an appendectomy and in 1918 he had had the "flu." He did not recall any other specific illnesses in the past. For a number of years the patient had had a productive morning cough which he attributed to smoking. In May 1940 his cough became more marked. At about the same time he lost his appetite and began to lose weight and strength. He also began to have night sweats. The patient consulted a physician; a chest roentgeno-

gram was taken, and a diagnosis of tuberculosis was made. Immediate admission to a sanatorium and induction of artificial pneumothorax were advised.

The significant physical findings on admission to the sanatorium were moderate congestion of the pharynx, deviation of the nasal septum to the right with beginning atrophy of the mucosa, markedly retracted and thickened right ear drum, and slightly retracted left ear drum. The lungs and heart were entirely negative. Blood pressure was 106 mm. Hg systolic and 70 mm. diastolic. Except for a linear scar over the abdomen, at McBurney's point, the remainder of the physical examination showed nothing noteworthy.

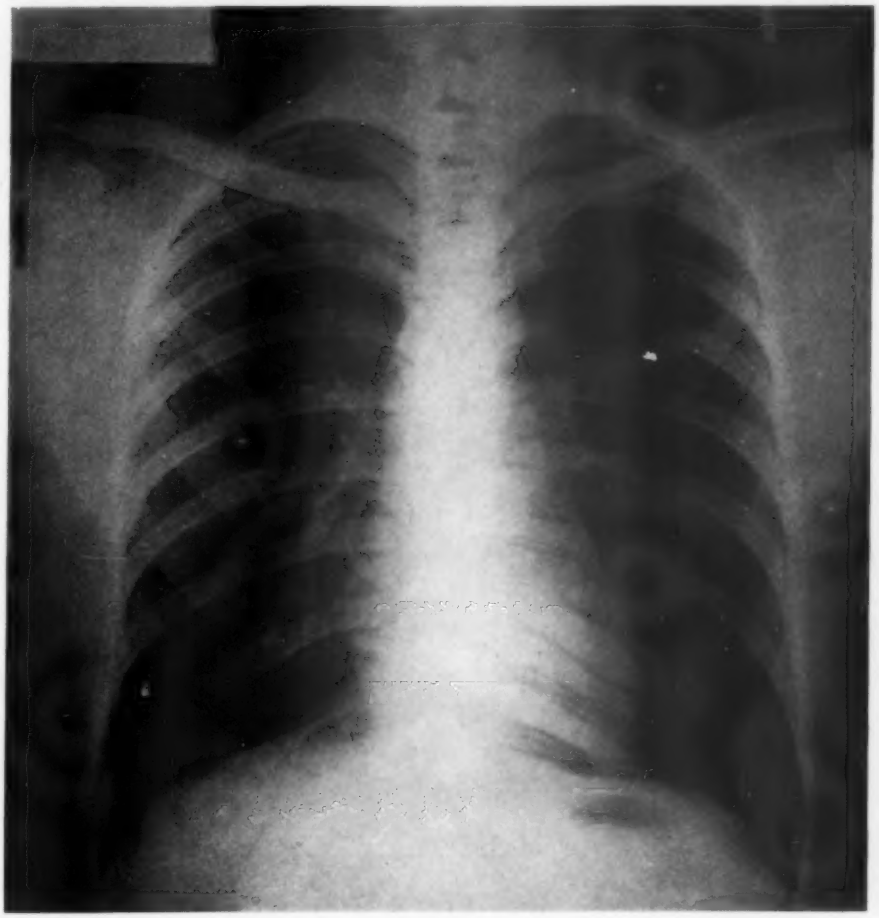

FIG. 7. (Case 3.) Roentgenogram taken August 10, 1933. Complete clearing of the infiltration in the right lung.

Laboratory Data. July 17, 1940. Urinalysis negative. The blood count showed: hemoglobin, 90 per cent; red blood cells, 4,560,000 per cu. mm.; white blood cells, 10,700 with polymorphonuclears, 43 per cent; lymphocytes, 55 per cent; monocytes, 1 per cent and eosinophiles, 1 per cent. Erythrocyte sedimentation rate, 12 mm. in 60 minutes. Kahn test was negative. Non-protein nitrogen 30 mg. in 100 c.c. of blood.

Six sputum examinations, including three of concentrated sputum, and one culture did not reveal the presence of tubercle bacilli. The vital capacity was 3200 c.c. An electrocardiogram showed low voltage of the Q R S complexes in all three leads, an isoelectric T_3, and left axis deviation.

Roentgenograms. A chest roentgenogram (figure 8), taken on July 2, 1940 (prior to admission), showed infiltration in the right upper lobe with an area of

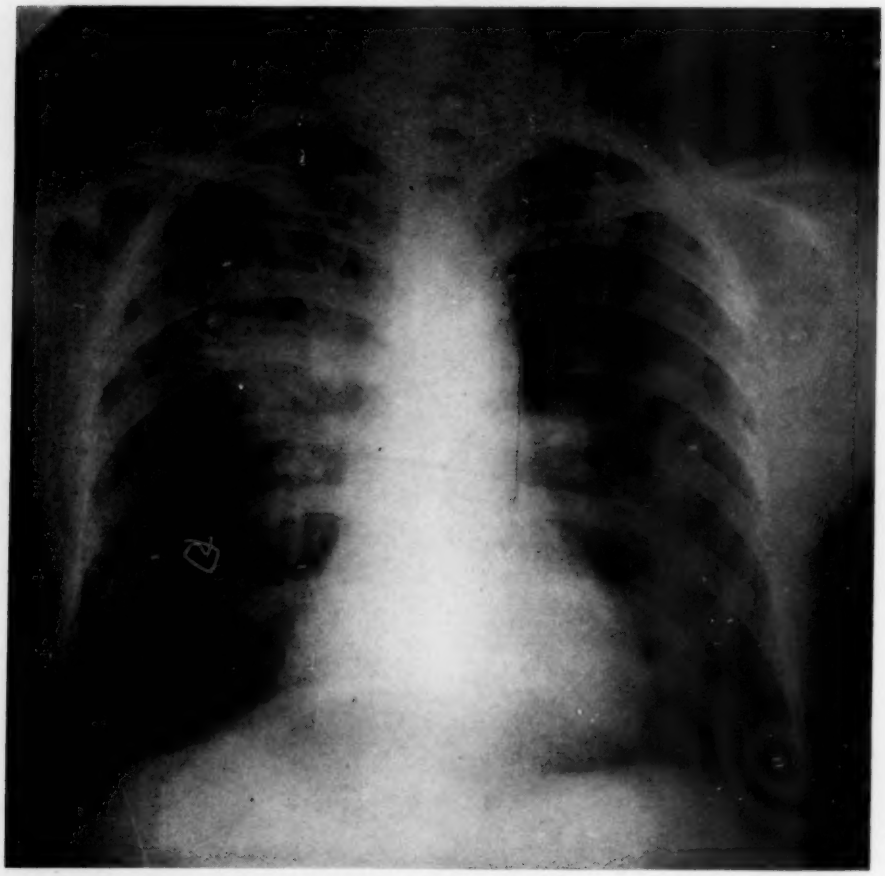

FIG. 8. (Case 4.) Roentgenogram taken July 2, 1940. Infiltration in the right upper lobe with an area of rarefaction suggestive of cavitation at the level of the second anterior rib.

rarefaction suggestive of cavitation at the level of the second rib anteriorly. The left lung was negative. The roentgenogram taken on admission to the sanatorium, on July 13, 1940, showed infiltration in the right second interspace external to the hilus region. There was no evidence of rarefaction, and the left lung was negative. A roentgenogram (figure 9), taken on August 20, 1940, showed almost complete clearing of the infiltration in the right lung, leaving a few fibrotic strands external to the hilus region. A roentgenogram taken on September 12, 1940, showed no change from the one taken on August 20, 1940.

Course. During the patient's stay in the sanatorium he ran an afebrile course and gained 18 pounds in weight. Except for a morning cough, productive of about

15 c.c. of mucopurulent sputum, he was symptomless. An attempt was made to obtain a bronchogram following lipiodol instillation. The bronchogram did not show any evidence of bronchiectasis. However, the bronchogram could not be considered conclusive because lack of coöperation on the part of the patient resulted in poor filling of the bronchial tree. Bronchoscopic examination was recommended but the patient refused to have that procedure performed because he claimed that he felt well and required no further treatment. He left the sanatorium against medical advice on September 13, 1940.

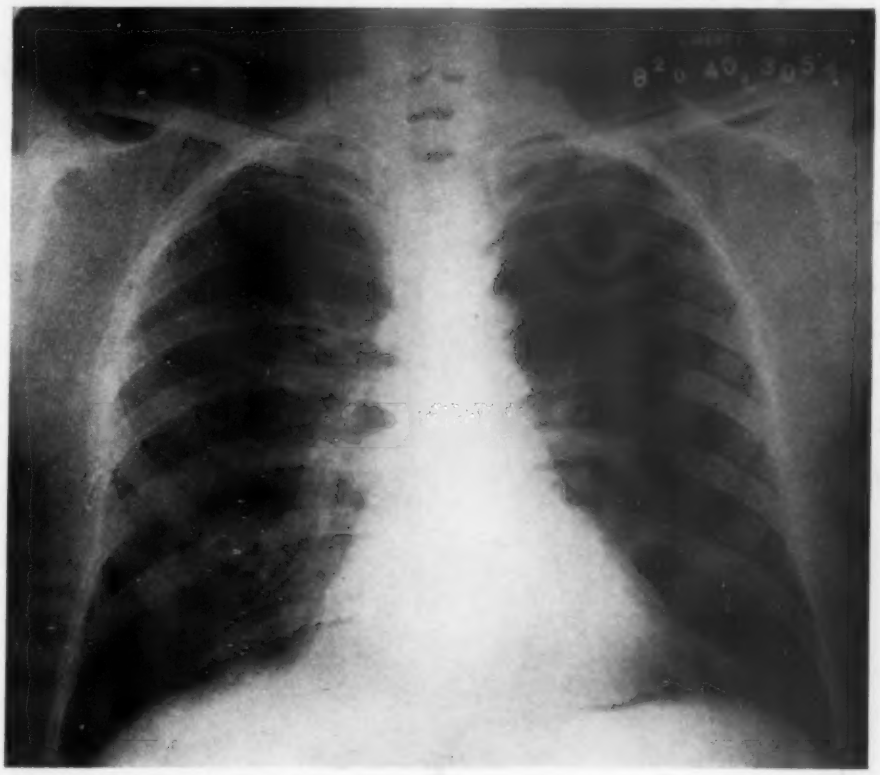

FIG. 9. (Case 4.) Roentgenogram taken August 20, 1940. Almost complete clearing of the infiltration in the right lung; no evidence of rarefaction.

Comment. It is obvious that the infiltration in this patient's right lung was not tuberculous in origin. Although conclusive evidence is lacking, it is felt that this patient had had a bronchial infection for some time and that the density in the right upper lobe, seen on the first roentgenogram (figure 8), was due to lobular atelectasis resulting from temporary plugging of a bronchus. It is difficult to account for the suggestive cavity in the right upper lobe. It is possible that there was beginning necrosis in the lobular atelectatic area, the patient emptying the necrotic material spontaneously when plugging of the bronchus was no longer present.

Case 5. S. M. F., male, aged 39 years, a salesman, was seen by one of the present writers (E. S.) on July 18, 1939. On May 30, 1939, the patient was taken ill with a productive cough, slight elevation of temperature, and occasional mild wheezing, but no frank asthmatic attack. He consulted a physician who referred the patient to a roentgenologist. A roentgenogram of the chest was taken and a diagnosis of resolving pneumonia or tuberculosis in the right lung was made. The subjective symptoms

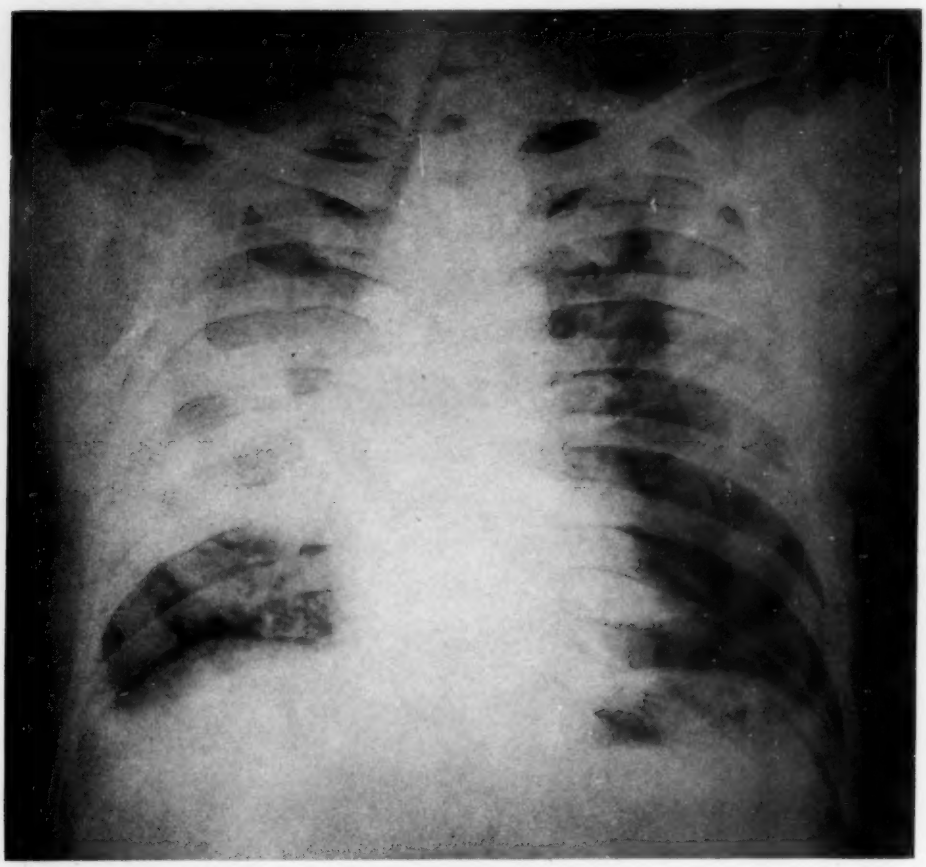

FIG. 10. (Case 5.) Roentgenogram taken May 31, 1939. Dense infiltration involving almost the entire right lung. Increase in lung markings throughout the left lung.

subsided in a few days. About one week after the onset of the present illness the patient had an attack of dyspnea which was diagnosed as bronchial asthma by his physician who administered adrenalin and ephedrine, giving the patient some relief. Immediately following this episode the patient began to cough again. He perspired freely, there was slight elevation of temperature, and he began to lose weight and strength. Another chest roentgenogram was taken; a definite diagnosis of tuberculosis was made; and the patient was referred to one of the present writers (E. S.).

The significant findings noted on the first examination (July 18, 1939) were harsh breathing over the left lung anteriorly and coarse râles posteriorly in the interscapular region. The left lung was clear. The heart was entirely negative. Blood

pressure was 110 mm. Hg systolic and 70 mm. diastolic. The spleen was not enlarged. Temperature was 99.5° F.

Laboratory Data. July 31, 1939. The blood count showed: hemoglobin, 85 per cent; red blood cells, 4,500,000 per cu. mm.; white blood cells, 14,200 with polymorphonuclears, 68 per cent; lymphocytes, 20 per cent; eosinophiles, 11 per cent and basophiles, 1 per cent. On August 21, 1939, the blood count showed: hemoglobin, 80

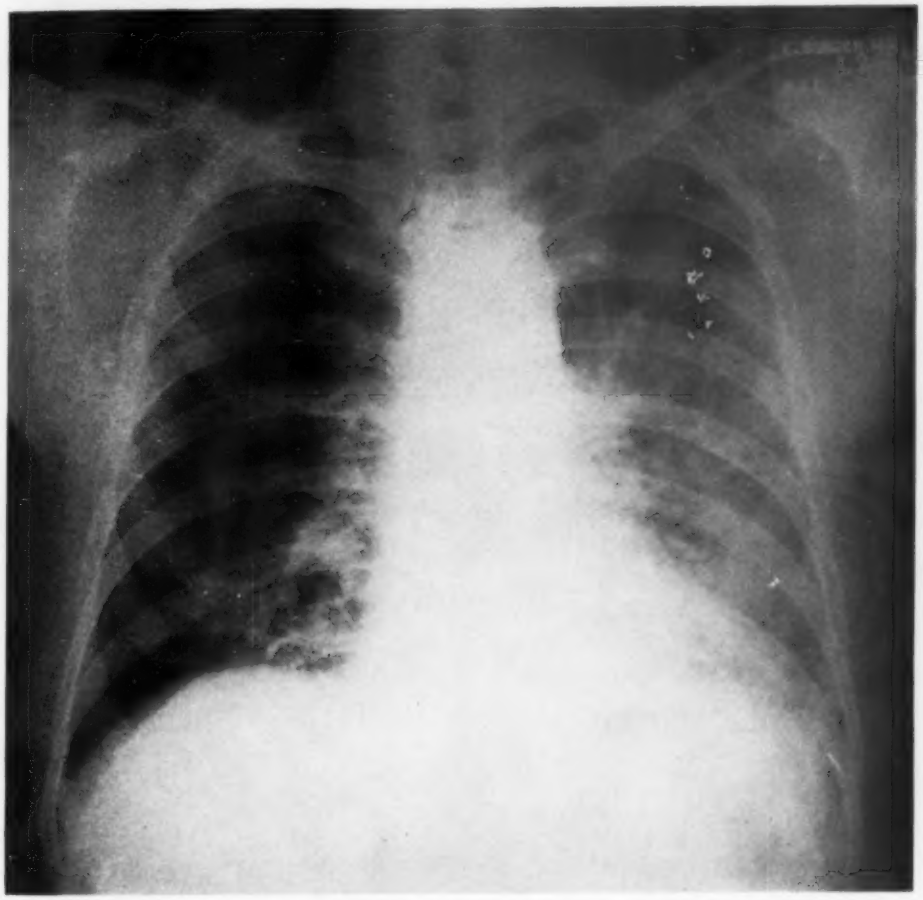

FIG. 11. (Case 5.) Roentgenogram taken July 31, 1939. Complete clearing of the infiltration in the right lung. Scattered infiltration throughout the left lung.

per cent; red blood cells, 4,650,000; white blood cells, 12,600 with polymorphonuclears, 64 per cent; lymphocytes, 21 per cent and eosinophiles, 15 per cent. Another blood count on October 23, 1939, showed: hemoglobin, 85 per cent; red blood cells, 5,100,000; white blood cells, 8,500 with polymorphonuclears, 76 per cent; lymphocytes, 19 per cent; monocytes, 2 per cent; eosinophiles, 2 per cent and basophiles, 1 per cent. A number of sputum examinations, including several of concentrated sputum, did not reveal the presence of tubercle bacilli. A search for fungi and spirochetes in the sputum gave negative results. A stool examination failed to show the presence of ascaris larvae.

Roentgenograms. A chest roentgenogram (figure 10), taken on May 31, 1939, showed dense infiltration involving almost the entire right lung. There was increase in lung markings throughout the left lung. On July 31, 1939, the chest roentgenogram (figure 11) showed almost complete clearing of the infiltration in the right lung field, but the left lung showed scattered infiltration throughout the lung field. Another chest roentgenogram (figure 12), taken on August 18, 1939, showed some clearing

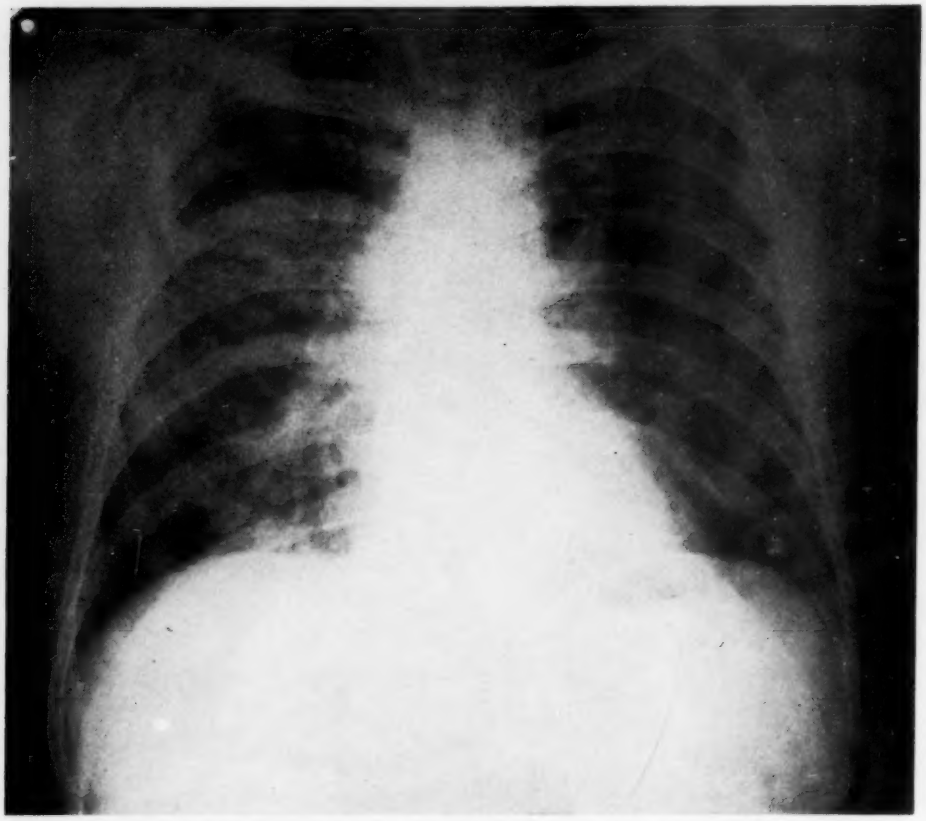

FIG. 12. (Case 5.) Roentgenogram taken August 18, 1939. Considerable clearing of the infiltration throughout the left lung. Reappearance of infiltration in the right lung.

of the infiltration throughout the left lung field. In the right lung, however, scattered infiltration throughout the lung, particularly in the second interspace, had reappeared. On September 15, 1939, a chest roentgenogram (figure 13) showed relatively little change in the right lung as compared with the previous film. In the upper half of the left lung field there was now evidence of dense infiltration. On September 29, 1939, the chest roentgenogram (figure 14) showed complete clearing of the infiltration in both lung fields. Chest roentgenograms taken on October 23, 1939, and January 20, 1940, showed no change from the film taken on September 29, 1939; no abnormal changes were noted.

Course. July 31, 1939. Temperature was elevated, occasionally as high as 101° F. The cough became spasmodic in character and the patient experienced difficulty in raising sputum. He complained of pain over the right side of his chest.

Examination revealed moist râles and rhonchi throughout the left lung; there were a few râles in the right lung. The patient was seen again on August 21, 1939, after two weeks' rest in the country. The temperature remained elevated, frequently to 101.4° F. There was a slight cough productive of scanty, odorless expectoration. He had no wheezing or asthmatic attacks but complained of a sense of oppression over the front of the chest. The râles and rhonchi had disappeared. He reported

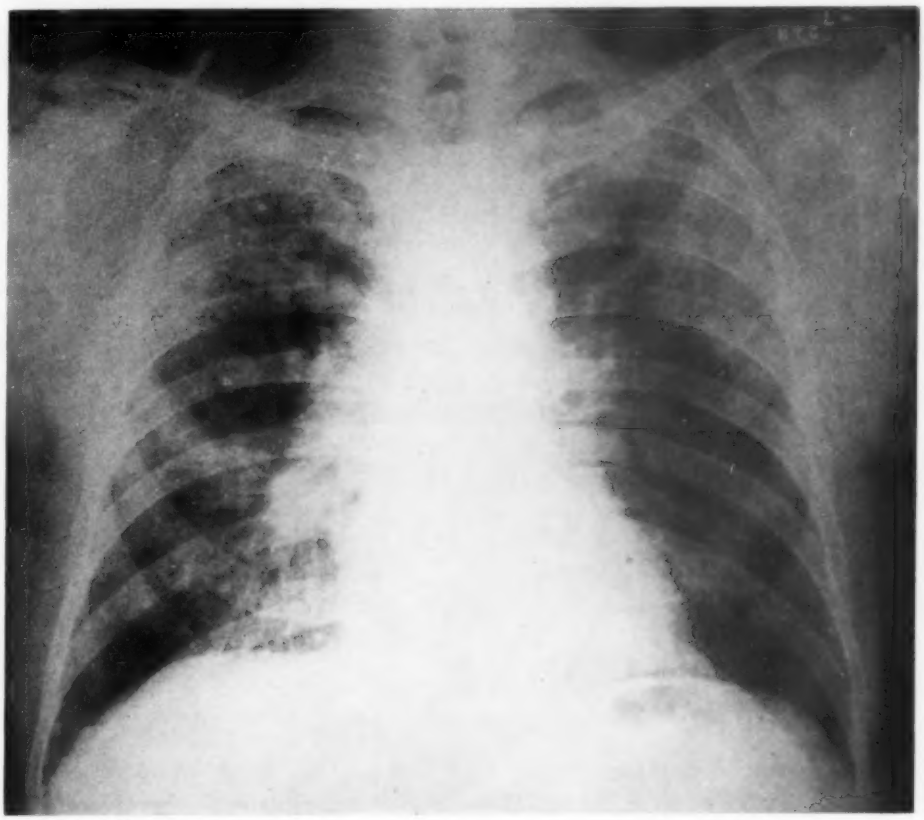

FIG. 13. (Case 5.) Roentgenogram taken September 15, 1939. Right lung relatively unchanged. Reappearance of dense infiltration in the left upper lobe.

again for examination on September 1, 1939. Except for a slight unproductive cough the patient was symptomless. He had gained four and one-half pounds in weight. Physical examination of the chest was entirely negative. On September 15, 1939, he had no complaints. He had gained five more pounds in weight. There were no abnormal physical findings. September 22, 1939. The patient continued to gain in weight. There was some edema of the left eyelid and supraorbital region which was thought to be due to some allergic manifestation. Otherwise, the physical examination was entirely negative and the patient was symptomless. October 23, 1939, the edema of the left eye lid had disappeared. Abnormal physical findings were absent and the patient claimed that he felt well. The patient returned for routine examinations in November 1939, January 1940, and was last seen in June 1940. He had returned to work in October 1939. He continued to gain weight and had no complaints. Physical examination remained negative.

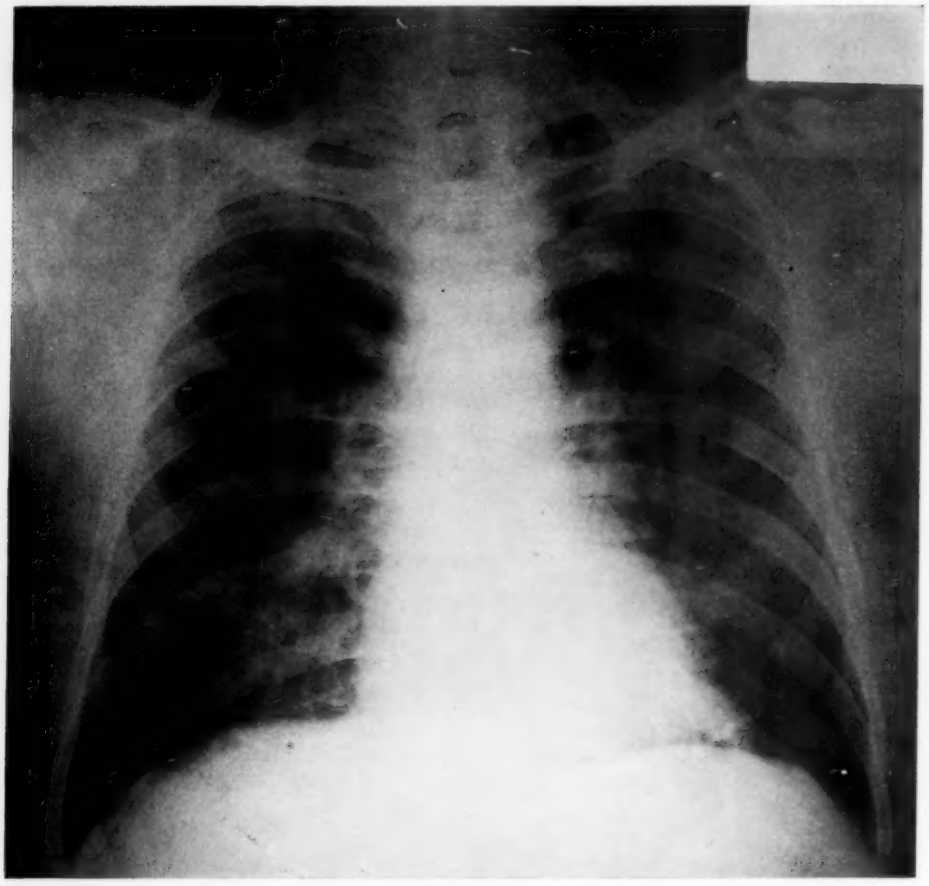

FIG. 14. (Case 5.) Roentgenogram taken September 29, 1939. Both lung fields clear.

Comment. This case presents an interesting clinical picture of transitory, migratory pulmonary infiltrations associated with eosinophilia. Except for the absence of cardiac manifestations and the migratory character of the pulmonary infiltrations there is a close similarity between this case and the first one presented. The infiltrations in both instances were not of a tuberculous nature. It is believed that the pulmonary manifestations in these two cases were on an allergic basis.

DISCUSSION

Cases 2 and 3 presented chest roentgenograms indistinguishable from roentgen pictures of pulmonary tuberculosis. Both patients had bronchopneumonia, probably caused by a filtrable virus. During the past several winters such cases have been not uncommonly observed. The roentgenogram at the onset of the illness, the symptoms and blood picture closely simulate the exudative type of tuberculosis. In order to arrive at a definite diagnosis, before instituting collapse therapy, it is wise, therefore, to take

serial chest roentgenograms and make a thorough search for tubercle bacilli in the sputum and aspirated gastric contents.

Although the diagnosis in case number 4 was not definitely established, the infiltration and rarefaction seen on the first roentgenogram (figure 8) were thought to be due to lobular atelectasis with beginning pulmonary necrosis as a sequence of bronchial obstruction. Similar roentgenograms which not infrequently need to be differentiated from pulmonary tuberculosis are seen in cases of pulmonary neoplasms and lung abscess. Bronchoscopic examination, serial roentgenograms and absence of tubercle bacilli disclose the non-tuberculous nature of the pathologic bronchopulmonary process.

Cases 1 and 5 present interesting problems in pathogenesis. In connection with these cases it is of interest to refer to reports by Smith,[3] Müller,[4] and Löffler,[5, 6] who described similar cases, and to review the latter report by Löffler in some detail. In 1936 he reported 51 instances of patients with transitory pulmonary infiltrations associated with eosinophilia in every case. The roentgenograms presented various types of densities described as follows: (1) large, more or less irregularly outlined densities which were unilateral or bilateral; (2) small infraclavicular infiltrations of the type described by Assmann; (3) multiple unilateral or bilateral circular densities; (4) sharply defined densities situated in the right middle lobe; (5) infiltrations indistinguishable from the adult-type of pulmonary tuberculosis. In the differential leukocyte count the number of eosinophiles ranged between 10 and 50 per cent. In some instances the eosinophilia reached a peak when the pulmonary infiltration had almost entirely cleared. Eosinophilia persisted for some time in some of the cases. There was no strict parallelism between the extent of the eosinophilia and the pulmonary infiltration. Some of the patients who had blood counts prior to the appearance of the pulmonary infiltrations showed no eosinophilia. Occasionally there was a leukocytosis up to 15,000 white blood cells. The sedimentation rate as a rule ranged between 8–15 mm. in one hour; in a few cases a more rapid rate was observed. Constitutional symptoms were mild or entirely absent. The clinical course was very benign, and the infiltrations on the roentgenograms cleared in three to eight days. In only one instance did pulmonary infiltration reappear, and that occurred one year after the original episode. Sputum specimens of all the patients were examined for tubercle bacilli with negative results in every case. All the patients were adults and most of the cases occurred during the months of July and August. In two instances the condition was noted in members of the same family. In 37 cases the tuberculin reaction was positive and in 13 instances a negative reaction was obtained.

Löffler discusses the pathogenesis of this clinical entity. He rules out pulmonary embolism with infarction, pneumonia, bronchial asthma with partial atelectasis, and pulmonary tuberculosis. He considered ascariasis as the etiology, but examination of the sputum and stools did not disclose the presence of ascaris larvae in a single instance. Löffler thinks that the

pathogenesis in these cases is similar to erythema nodosum; the lung reacts with an inflammatory exudate to a toxin. It is his impression that the pulmonary manifestation is on an allergic basis.

Cases 1 and 5 described by the present authors can be grouped with the clinical entity described by Löffler. Both patients had transitory pulmonary infiltrations associated with eosinophilia. The clinical picture in these two instances differed in some respects from the majority of cases in Löffler's series. The symptoms in the present cases were more pronounced and persisted for longer periods of time. The pulmonary infiltrations observed on the serial roentgenograms showed less rapid clearing, and in case 5 the infiltrations were of a peculiarly migratory character. However, it is suggested that the differences can be explained logically on the basis of a more intense and prolonged allergic response to some allergen. The agent producing the allergic reaction in the two cases presented was not determined. It should also be pointed out that Löffler did not observe cardiac manifestations in any of his patients; at any rate, he makes no mention of them. In case 1 there was evidence of right-sided cardiac strain. Here again, it can reasonably be assumed that because of the more pronounced allergic reaction the pulmonary exudate persisted for a sufficient length of time to produce increased resistance in the pulmonary circulation resulting in right ventricular strain. With the absorption of the pulmonary exudate the heart returned to normal size.

Summary and Conclusions

1. Five cases of non-tuberculous pulmonary disease mistaken for pulmonary tuberculosis are presented.

2. Reliance on a single chest roentgenogram for diagnosis frequently leads to error.

3. When tubercle bacilli cannot be found in the sputum or aspirated gastric contents by all methods of examination, including cultures and guinea pig inoculation, it is extremely unlikely that the bronchopulmonary disease is of tuberculous etiology.

4. The clinical picture and pathogenesis of pulmonary infiltrations associated with eosinophilia are discussed.

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CASE REPORTS

INTRATHORACIC LIPOMA; A CASE REPORT*

By Oscar Swineford, Jr., M.D., F.A.C.P., and Charles J. Harkrader, Jr., M.D., *University, Virginia*

The subject of intrathoracic neoplasms has been reviewed recently by Heuer and his associates.[1, 3] They summarized all case reports to date. McCorkle, Koerth, and Donaldson [2] tabulated the most common symptoms and signs of the cases of thoracic lipomata of each type reported before 1938.

The following case of intrathoracic lipoma is reported because it is the second in which asthma was the chief complaint,[2] and because it is the eighth largest of the 25 wholly intrathoracic lipomata now on record.

Case Report

A 62 year old white single male was admitted in severe status asthmaticus and congestive failure of 10 days' duration.

Present Illness. A transient acute respiratory infection had precipitated an attack of asthma, which was followed promptly by congestive failure. He had had to sit up in a chair for 96 hours prior to admission.

Systems History. The patient had had asthma for 25 years, usually precipitated by acute respiratory infections to which he was unduly susceptible. In October 1937, he was bronchoscoped by Dr. Porter Vinson of Richmond, Virginia, with marked relief of a severe episode of asthma until April 1939, when he had to be bronchoscoped a second time. He was markedly, but not completely, relieved again until two weeks before admission. Bilateral bronchospasm with moderate serous secretion, but no bronchostenosis, was noted both times.

He had had palpitation for 10 years, hypertension for eight years, dyspnea on exertion for five years, orthopnea for four years, and an anginal attack two years before admission. He had had a few convulsions since 1935. He had had no congestive failure until his final illness.

Other symptoms were irrelevant.

Physical Examination. The patient was having severe asthma. He was cyanotic. There were signs of moderate congestive failure. In the base of the right lung there were dullness and markedly diminished intensity of tactile fremitus and of the voice and breath sounds. The heart seemed slightly enlarged to the left. There was moderate arteriosclerosis of the peripheral and retinal arteries. His venous pressure was 170 mm. of water. His blood pressure was 170 mm. Hg systolic and 90 mm. diastolic. Other physical findings were irrelevant.

Course in Hospital. Adrenalin, caffeine, seconal, mercupurin and theamin relieved his alarming acute symptoms. He was digitalized. His venous pressure became normal. His blood pressure dropped to 160 mm. Hg systolic and 75 mm. diastolic, but he continued to have moderately severe asthma.

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On the fourth day he had a Jacksonian convulsion. The aura were twitching of the left arm and jerking of his head to the left.

He was bronchoscoped on the sixth day. Thick tenacious secretion was aspirated from the trachea and the bronchi. The bronchi appeared partially collapsed. The orifice of the right middle lobe bronchus was dimpled and narrowed to about 2 mm.

He had a severe attack of asthma, with shock, immediately after the bronchoscopy. He remained semicomatose with frequent periods of Cheyne-Stokes respiration, cyanosis, and pulmonary edema for six days, when he died.

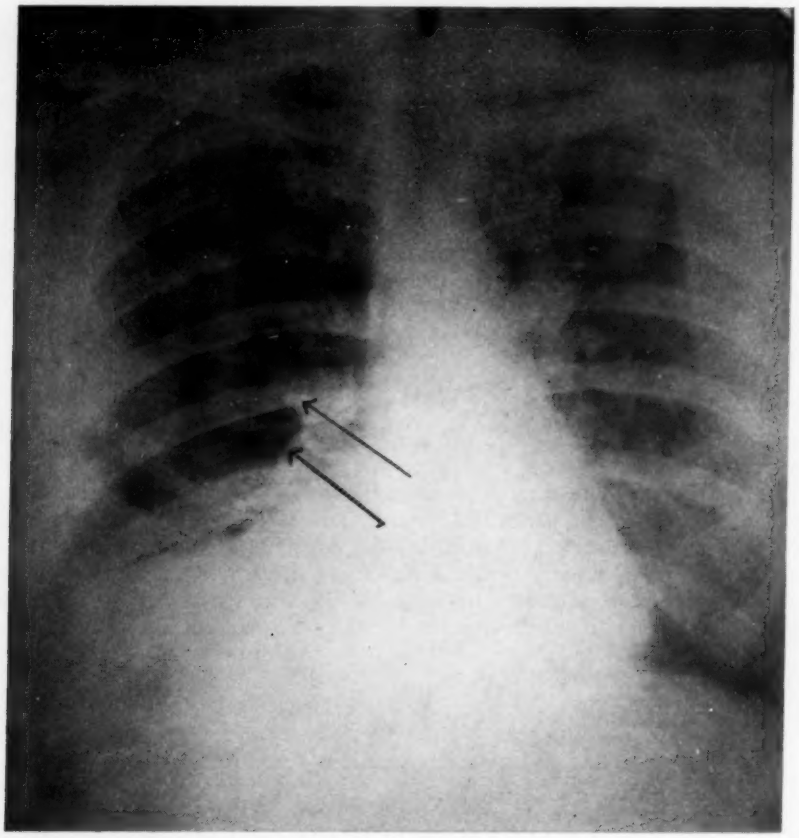

FIG. 1. October 5, 1937. (Dr. Fred Hodges, Richmond, Virginia, Roentgenologist.) Note two rounded masses in the right hilar zone and the apparent elevation of the right diaphragm, with decreasing density of the shadow from the midclavicular line to the periphery.

Special Examinations. Staphylococcus albus non-hemolyticus, a chromogenic micrococcus, and *Streptococcus viridans* were cultured from the sputum. The electrocardiogram showed evidence of myocardial damage. No significant abnormalities were noted in routine examinations of the urine, blood urea, hemoglobin, red and white blood cells, blood smear, blood Wassermann and Kahn tests, and roentgenograms of the sinuses.

The roentgen-ray examinations of the chest were most interesting. Dr. Fred Hodges of Richmond, Virginia, in October 1937 had reported (figure 1): "The left side is negative except for very broad hilum shadows. On the right side the dia-

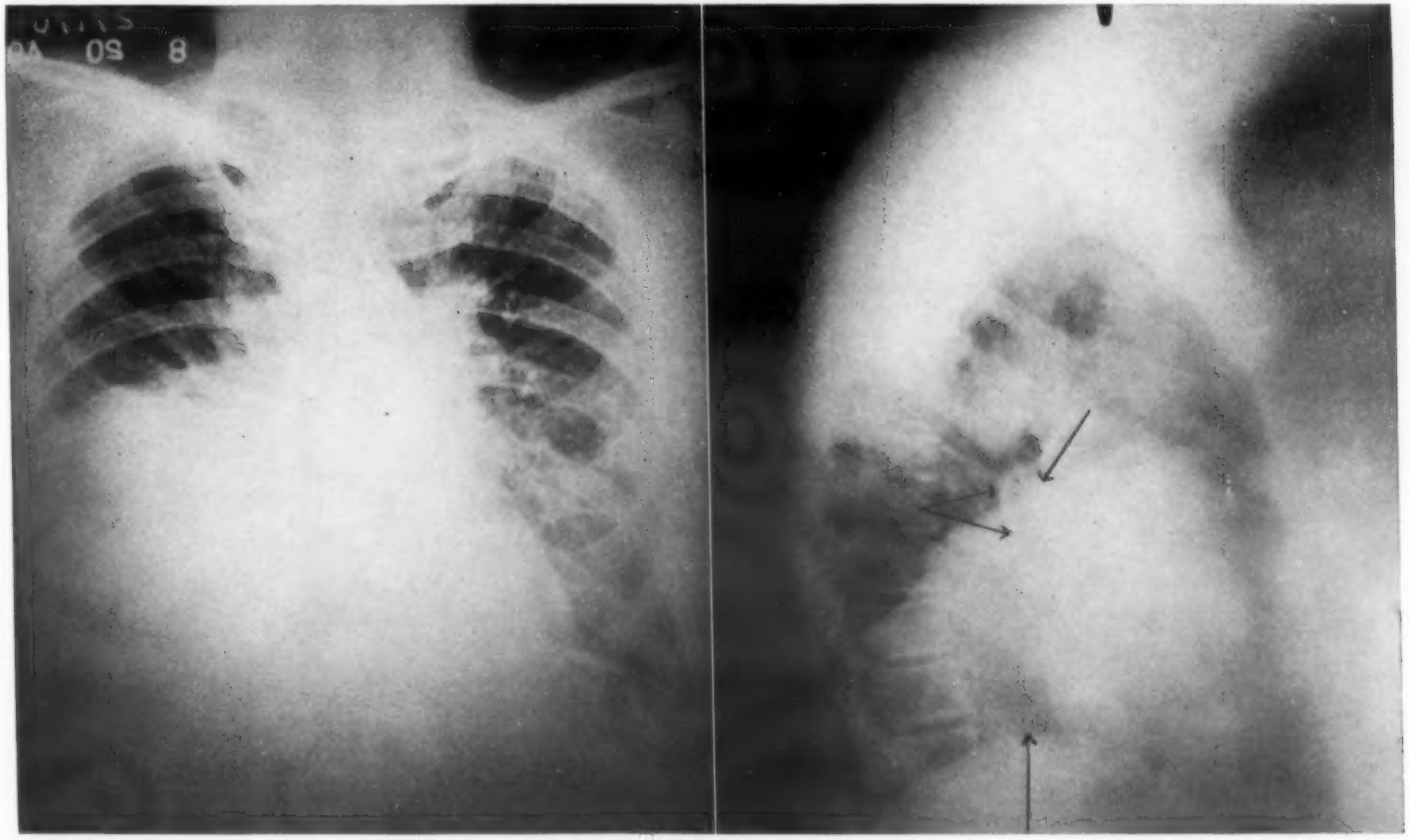

FIG. 2. August 20, 1940. The anterior-posterior films show a marked interim increase in the size of the tumor shadow, without the decreasing density from the center to the periphery noted in figure 1. The lateral view shows atelectasis of the middle lobe and an irregular upper border of the tumor. Note the atelectasis extending below the upper border of the tumor. Both are on the right. This should have suggested a mass lesion and not an elevated diaphragm.

phragm is elevated. There are two masses at the hilum, the larger being about 3 cm. in diameter. The changes should be due to atelectasis or possibly a growth at the hilum."

Dr. Vincent Archer, University, Virginia, interpreted films (figure 2) taken during the final illness as follows: "Marked opacity in the right base up to the level of the fourth rib anteriorly. There is an accentuation of the lung markings throughout

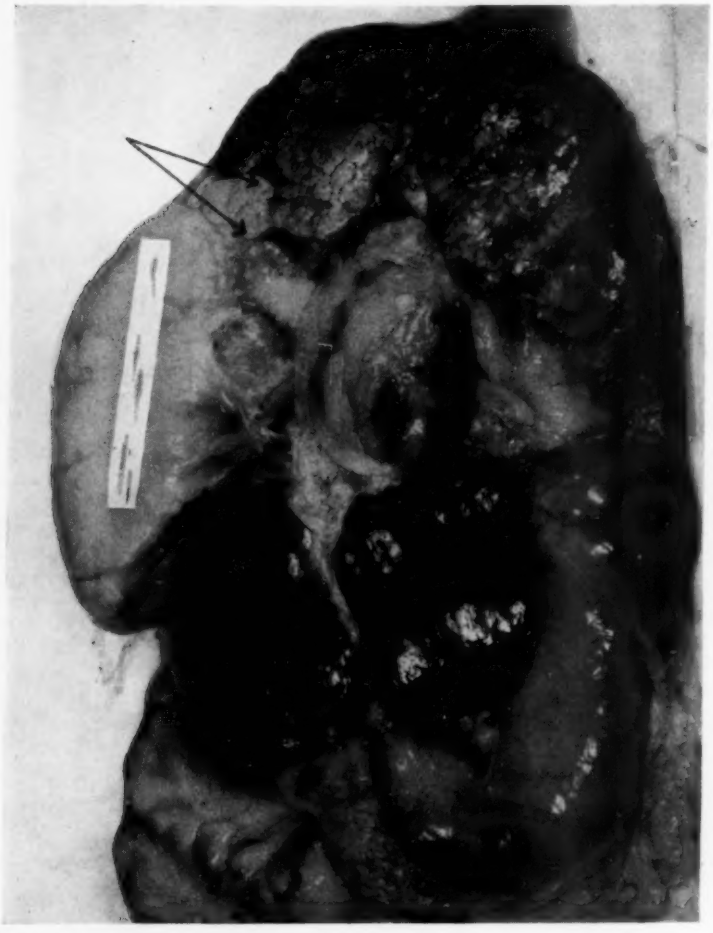

FIG. 3. The lipoma in its relation to the liver, heart and lungs. Note the narrow, collapsed, pale middle lobe. The upper and lower lobes are compressed also.

both lungs with calcium deposits in the left hilus zone. A lateral view shows the diaphragm elevated anteriorly mainly. There is thought to be definite atelectasis of the middle lobe which probably accounts for at least part of the elevation and the density of the right base. The lung markings running into the right upper were quite markedly accentuated in the lateral view."

Postmortem examination showed a large lipoma filling the base of the right thorax (figure 3). It was free except for a filmy attachment to the right mediastinal pleura. It weighed 2310 grams. Its longest diameter was 26 cm. The right lung was

displaced upward. The middle lobe was completely atelectatic. It was unpigmented, suggesting non-function of long standing. The orifice of the middle lobe bronchus was marked only by a small dimple. About one-third of the right lower lobe was atelectatic. In both lungs there was patchy consolidation with mucopurulent material in the bronchi. The left lung was emphysematous and covered with old adhesions. The mediastinum was not displaced. The heart weighed 550 grams. Both ventricles were slightly hypertrophied but not dilated. There was no chronic passive congestion. There was some pulmonary and peripheral arteriosclerosis. Microscopic examination of the tissues added nothing. Other findings were irrelevant.

Discussion

It is not necessary to assume that the lipoma was a primary cause of the asthma. Such marked relief, twice, from bronchoscopy would be hard to reconcile with this assumption. Besides, he had had asthma for many years whenever he had acute respiratory infections. Then, too, bronchial stenosis is a well recognized cause of asthma. The stenosis of the middle lobe bronchus in this case was apparently inflammatory in origin and not from direct external pressure. The absence of pigment, suggesting long standing absence of middle lobe function, further complicates the interpretation of the rôle of the lipoma as a cause of the asthma. It is interesting to point out, however, that McCorkle, Koerth, and Donaldson described signs or symptoms of asthma of some degree in five of the 19 cases which they reviewed, although they did not use the term asthma except in their own case.[2]

A review of the roentgenograms (figure 2) of the chest during the final illness suggests the presence of a mass above the diaphragm. They do not, however, have the one feature suggestive of an intrathoracic lipoma, namely, diminishing density of the shadow from the center toward the periphery. This feature was present to some degree in the films taken in 1937 (figure 1).

Summary

This is the twenty-fifth report of a wholly intrathoracic lipoma. It was not diagnosed clinically. Asthma was the chief complaint. Relevant postmortem findings are presented.

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BENIGN HEPATOMA; REVIEW OF THE LITERATURE AND REPORT OF A CASE *

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Local hyperplastic processes of the liver may manifest themselves variously in the form of a solitary focus of congenital origin in a normal liver, as multiple nodular hyperplasia, or in the guise either of a solitary or multiple adenomata. All these pathological conditions may occur indiscriminately with or without concomitant cirrhosis. Occasionally, benign tumors resulting from simple hypertrophy may eventually assume a malignant character.

In a dissertation submitted in 1910, Monier-Vinard [1] described a so-called new type of primary tumor of the liver, for which he proposed the specific and exclusive title of hepatoma. The latter he defined as a benign neoplasm of the hepatic parenchyma arising chiefly from liver-cord cells, ordinarily single but sometimes multiple, and most common in adults. This designation was suggested as a substitute for the less exact terms of adenoma of the liver and multinodular hyperplasia employed by previous writers on the subject.

However, at present considerable confusion exists concerning the appropriate use of the expression *hepatoma*. For example, primary epithelial tumors of the liver are correctly designated by Swalm and Morrison [2] as hepatomata when they are derived from liver cells, and as cholangiomata when they originate from intrahepatic bile-duct cells. A third group which arise from both liver cells and bile-duct cells they denominate mixed tumors. On the contrary, Ewing [3] includes under the classification of hepatoma, the benign form, adenoma, and the malignant forms, adenocarcinoma and carcinoma of the liver.

Solitary adenomata derived from liver cells are seldom observed, and their clinical differentiation from cholecystitis and lithiasis is often difficult. Although they are believed by some authorities to be of congenital origin, it is also regarded as probable that acquired lesions may occasion neoplastic overgrowth of isolated portions of the liver. Multiple adenomata involve a hyperplasia of liver cells and frequently are accompanied by a cirrhosis which dominates the clinical picture. The important rôle assumed by cirrhosis in the etiology of these latter tumors is ascribed to the compensatory hyperplasia induced by the antecedent hepatic stasis. This occurs quite commonly and produces these multiple adenomata of cirrhosis. Certain solitary tumors of the liver are thought to be due to interference with the supply of blood to the organ.

In typical solitary adenoma the veins are not invaded, and its benign character is attributable to its encapsulation. The transitional forms intermediate between adenoma and adenocarcinoma are distinguished chiefly by invasion of the veins, gradual progression beyond their capsule, and multiplication of tumors. The primary tumor generally consists of cords, tubes, and alveoli markedly resembling the structure of the liver. In occasional instances all three of these elements are encountered in a single tumor. Very often the neoplasm contains strands of cells which it is difficult to differentiate microscopically from the normal tissue. The cells are granular and acidophile, or very fatty. The stroma is composed mainly of capillaries.

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Benign tumors of the liver rarely exhibit symptoms unless they become sufficiently voluminous to cause mechanical pressure within the organ itself or upon the adjacent structures. The concomitant ascites, hematemesis, and thrombosis of the portal vein which are observed are related to the associated cirrhosis. Because of their failure to present a definite clinical syndrome, non-malignant hepatic tumors are usually discovered either by accident during the life of the patient or else only at autopsy.

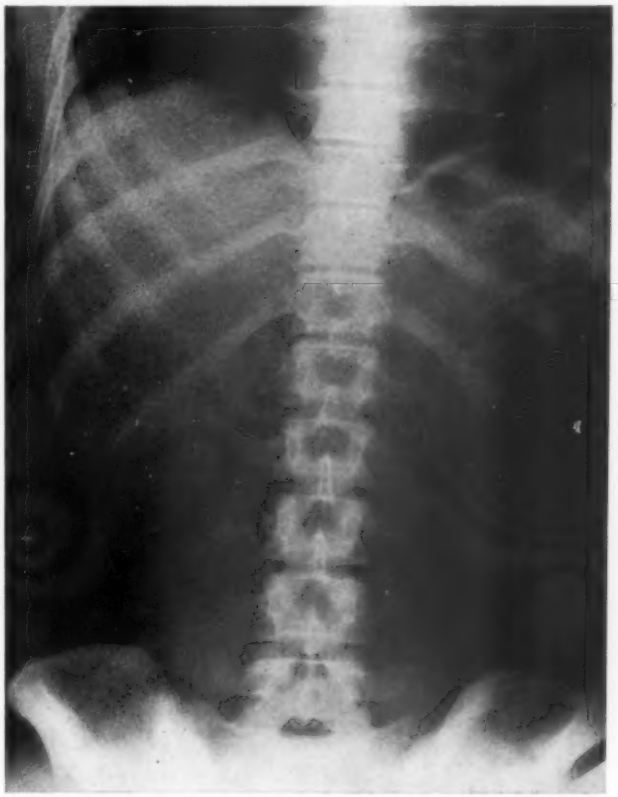

FIG. 1. Flat plate of abdomen showing shadow of tumor.

Unless they are large and productive of a considerable degree of discomfort, benign tumors of the liver seldom require treatment. Nevertheless, as in all cases of abdominal tumor, if there is even the slightest doubt concerning the diagnosis, an exploratory operation is always recommended in order to exclude the possibility of malignancy.

The purpose of the present communication is to record a case of true benign hepatoma and to include also a brief survey of those previously published. The comparative infrequency of benign tumors of the liver is attested by the fact that apparently only 58 cases have thus far been reported in the medical literature of the entire world. In 1908, Keller [4] presented a comprehensive tabular summary of the available data in the 55 cases contributed during the preceding

half century under the general title of adenoma. Among the patients comprised in this group, the youngest was a female aged nine, and the eldest a male of 80. Cirrhosis of the liver was present in 10 instances. In 18 the tumors were multiple, whereas in six the hepatoma was solitary. Encapsulation was complete in three and partial in eight. Clinical symptoms of obstruction of the portal circulation with ascites were noted in 11 cases, all of which terminated fatally within a few months following the onset of intense icterus, splenic tumor, and progressive marasmus. Similar symptoms were observed in two other instances in which death occurred after a period of illness ranging from several months to about one year.

FIG. 2. Mass removed at operation.

Monier-Vinard [1] in 1910 reported a classic case of benign hepatoma in a man of 54, with a history of chronic alcoholism of from 20 to 30 years' duration, and clinical symptoms of dyspepsia, emesis, diarrhea, and aversion toward solid foods.

For several months prior to consultation the patient had remarked a progressive increase in volume of the abdomen. At the time of admission to the hospital he complained of extreme debility and of pain in the upper abdominal region, especially after meals. On physical examination the abdomen appeared greatly enlarged. The spleen was palpable over an area approximately equivalent in extent to the palm of the hand. Palpation in the hepatic region revealed upon the surface of the liver very numerous and extremely hard irregularities which suggested the diagnosis of simple cirrhosis or the possibility of a secondary neoplasia of the liver. No sugar and only slight traces of albumin were found on urinalysis. A considerable augmentation of the ascites was noted upon the second day following admission, with a corresponding increase in the size of the abdomen. Fourteen liters of blood-stained fluid, which subsequently yielded an abundant precipitate of red corpuscles, were evacuated by puncture.

Two weeks later the patient was attacked by violent colic and passed about half a liter of extremely fetid, reddish brown diarrheal matter composed of what proved on microscopic examination to consist of greatly altered red corpuscles. On the day after this intestinal hemorrhage, a recent disseminated purpuric eruption was observed, particularly upon the lower limbs and over the trunk and upper members. During the week which followed, the general condition of the patient became aggravated, primarily in consequence of an exceedingly copious intestinal hemorrhage. Four days later death occurred in progressive coma.

Microscopic examination of the liver showed that the latter was the seat of a cirrhosis and of a neoplasm whose cells presented the characteristic arrangements of cords and strands of from two to three cells in thickness, and of nests of cells

FIG. 3. Tumor cut open to show gross appearance of tissue.

that simulated the formation of acini. The tumor cells resembled liver cells in their cytoplasm and in the size of their nucleus but were more hyperchromatic, and some of them were in a state of active mitosis. An epithelial type of cell with a large amount of cytoplasm and giant cells of epithelial origin, likewise abundantly supplied with cytoplasm, were also encountered. The entire tumor presented a highly vascular aspect, the newly formed capillaries which pervaded the section exhibiting the appearance of granulation tissue. The stroma consisted of partly degenerated connective tissue. Along the margin of the tumor there was a clearly defined capsule of connective tissue.

The etiology of hepatoma was attributed by Monier-Vinard [1] to chronic inflammatory irritation coexistent with cirrhosis. He classified hepatoma as the prototype of a new group of tumors which might be described by the term *organomas*. This group appeared to him to be represented by myeloid leukemia and lymphoid leukemia, and to include also tumors which developed in organs or tissues derived from the mesoderm.

A rare instance of the occurrence of a solitary liver-cell adenoma or hepatoma in childhood was recorded in 1923 by Shaw.[5]

Ten days prior to admission to hospital, a boy aged 13 was attacked suddenly by severe abdominal pain, followed by the appearance of a swelling in his right side, the pain having persisted, though with diminishing intensity, until the fourth day preceding admission. Physical examination revealed in the right hypochondrium a large nodular swelling apparently continuous with the liver and the right kidney. Laparotomy was performed, and a large lobulated tumor was found to occupy a considerable proportion of the right lobe of the liver. The rest of the liver appeared normal, with no cirrhosis, no secondary deposits in the peritoneal sac, and no ascites. The tumor was removed together with the attached gall-bladder. Recovery was uneventful, and the patient was discharged three weeks after the operation.

The surface of the tumor was covered only by the distended capsule of the liver. Its upper surface was rendered irregular by deep branching furrows, whereas the lobules upon its anterior surface were separated by sharp depressions, one of which divided this portion of the tumor into two parts. From a central area of fibrosis numerous broad strands of connective tissue radiated outwards, gradually became thinner, and finally disappeared near the periphery, which was more markedly cellular in aspect than the glistening fibrous center. A few scattered blood vessels which showed no thrombosis were seen in the fibrous strands, but no bile ducts were discerned. At the junction of the nodular portion with the principal mass of the neoplasm there were several opaque, white, soft, circumscribed areas of tumor tissue, which were highly cellular, devoid of bile staining, and encapsulated by fibrous tissue. The posterior and lateral margins of the neoplasm presented a clearly defined edge but were not encapsulated. The adjacent hepatic tissue was fatty and slightly compressed, but there was no evidence of cirrhosis, no thrombi in vessels, and no bile staining. The gall-bladder was normal.

Microscopic examination of a part taken from the right posterior region of the growth showed that numerous broad strands of fibrous tissue separated the tumor cells into masses of irregular size and shape, this dense, rather hyaline stroma containing comparatively few cells. Thinner and more delicate strands arose from the principal bands and passed into the parenchyma. Although some of the neoplastic cells resembled those of normal liver in size, shape, and general structure, the majority were quite atypical, with a large, round, oval, or lobulated nucleus, thicker nuclear membrane, and a nucleolus (occasionally multiple) larger than in the normal liver cell. Many of the nuclei were hyperchromatic, and others were markedly altered by nuclear vacuolation. Multiplication apparently occurred somewhat by direct division, and mitotic figures were scanty. The cytoplasm exhibited wide variation with respect to staining capacities in the individual cells. A certain proportion of cells formed bile in the form of green granules or blocks within the protoplasm.

Portions taken from several other parts of the tumor for examination presented generally a similar histological structure, except for the circumscribed soft area from the junction of the nodular part of the tumor with the main growth, which was in marked contrast to all other parts examined. It consisted of strands of cells arranged in a distinctly trabecular formation which resembled more closely the adenomatous type seen in the hyperplastic nodules of cirrhosis than the normal liver. The tissue was distinctly vascular, and a network of branching capillaries passed between the trabeculae. There was very little fibrous tissue. The tumor cells bore a striking resemblance to normal liver cells but were somewhat larger, though fairly uniform in size and shape. The nucleus was larger, the nucleolus more prominent, and the cytoplasm less granular and more chromophilic. Cells with two or more nuclei were exceedingly rare. Intercellular canaliculi were common but contained no bile. The cells lay close to the capillaries, but there was no invasion of the larger vessels in the stroma. Mitotic figures were rare. There was no formation of bile and no bile

ducts. Nuclear vacuolation and hydropic degeneration were virtually absent, but some cells contained small round hyaline bodies in their cytoplasm.

The presumption of the origin of the tumor from liver cells was thus confirmed by the appearance of the neoplastic cells, their capacity to form bile, and their trabecular arrangement in places. The neoplasm was regarded as a typical example of the rare group of tumors of the liver which are characterized by occurrence in infancy or childhood, the presence of a solitary growth, and the

FIG. 4. Photomicrograph of section of tumor.

absence of cirrhosis or other associated pathological alteration which might explain an initial hyperplasia of liver cells. There was no evidence whatever of a development from epithelium of the bile ducts. Genesis of the tumor from a cell-rest of congenital origin was also considered as a possibility in the case under consideration.

More recently an extraordinary case of hepatoma with recurrence five years after the original operation was reported by Glennon and Byrne.[6]

At the time of admission to hospital the patient, a man aged 49, suffered from pain in the right upper quadrant of the abdomen and in the region of the left kidney,

and from eructation. The onset of pain and digestive disturbance dated from a fall sustained eight years previously, when four ribs on the right side were fractured. Since then the pain had been practically constant but in nowise associated with the ingestion of food. Loss of weight had been considerable. On examination it was observed that the abdomen was somewhat distended, particularly on the right side, and that a fairly large, soft, slightly tender mass apparently connected with the liver extended downward almost to the umbilicus and backward toward the right kidney. The mass was smooth, fluctuant, and regular in outline. Fluoroscopic and radiographic studies of the gastrointestinal tract proved negative. Exploratory laparotomy disclosed on the left lobe of the liver a mass the size of a large grapefruit, entirely free from adhesions, and of grayish color. A number of blood vessels were seen in the wall of the mass. Except for this mass the liver was, like the gall-bladder, normal. An incision into the most prominent part of the mass revealed a soft, grayish tissue evidently in process of degeneration. At this juncture profuse bleeding from the wall of the mass necessitated the insertion of a large pack into the cavity, the contents of which were thereupon removed, and the wound was closed with the pack protruding from its upper angle. Following immediate microscopic examination the tumor was declared malignant. Loss of the disintegrated mass removed as described rendered subsequent microscopic study impossible. Despite the unfavorable prognosis, healing of the wound and general improvement ensued within a few weeks.

About five years later the patient was again admitted with a recurrence of the tumor, which this time was located in the right upper quadrant of the abdomen and was as large at least as the original growth, but apparently extended superiorly toward the ensiform cartilage. There was simultaneous recurrence of former symptoms of loss of weight, anorexia, and eructation. The abdomen was reopened through the old scar, and a tumor the approximate size of a grapefruit was found arising from the inferior and anterior surfaces of the left lobe of the liver. Adhesions were present between the abdominal wall and the tumor and even denser adhesions between the tumor and the posterior abdominal wall near the median line. The tumor was freed, the left lobe of the liver mobilized, and a complete lobectomy with removal of the attached tumor was performed. Convalescence was uneventful, and the patient was discharged in due course.

After six months of definite improvement, during which the patient remained under constant observation, the tumor reappeared, on this occasion outside the liver in the retroperitoneal region and on the left side of the abdomen. Deep roentgenotherapy of the now inoperable tumor afforded no relief, and death occurred 15 months later with all the phenomena of carcinoma. Autopsy revealed an extensive retroperitoneal mass which compressed the stomach and intestines superiorly and laterally but did not invade these organs. The liver was free from the tumorous growth and exhibited only the old scar of the lobectomy. No metastases were found anywhere.

Macroscopically the tumor removed with the left lobe of the liver was roughly conical in shape and measured 15 centimeters from apex to base, and eight centimeters in diameter, with about four centimeters of normal liver tissue attached to the base. The entire center of the mass consisted of disintegrated necrotic tissue which resembled closely that encountered on examination of the original tumor. Microscopic section showed tissue only moderately cellular, with numerous large and small areas of coagulative necrosis. The cells of the tumor itself, which exactly simulated liver cells in their cytoplasm and the size of their nucleus, exhibited the typical disposition into cords and strands, with clusters of cells highly suggestive of adenocarcinoma. The stroma of connective tissue presented scattered evidences of degeneration. Epithelioid cells with a divided nucleus and giant cells, also of epithelial origin, with a large single hyperchromatic nucleus, all containing large amounts of clear staining cytoplasm, were observed. Vascularization was well marked. The mass removed at autopsy resembled the original tumor macroscopically as well as microscopically.

In the opinion of Glennon and Byrne,[6] the foregoing facts demonstrate that the tumor in question arose from liver-cord cells, and commenced as a single encapsulated solitary tumor, namely, a hepatoma. Although its histological characteristics apparently identified it as a partly differentiated malignant tumor, encapsulation of the original neoplasm was believed by them to exclude typical malignancy irrespective of the histological picture which was presented.

The paucity of examples of benign hepatoma, as well as the somewhat unusual features presented by the case about to be reported, appeared to afford ample warrant for its publication.

Case Report

A married woman, aged 38, on June 11, 1940, applied for treatment of a mild acute upper respiratory infection. During the course of her conversation the patient remarked that for the past fortnight she had had a sense of consciousness of her right upper abdomen. There was no pain, discomfort, or any other symptoms. On palpating her abdomen she thought she had felt a mass in the right upper quadrant. Apart from the slight discomfort incident to her respiratory infection, she felt quite well. Her appetite was excellent, bowels regular, and sleep sound. She gave a personal history of chronic sinusitis and chronic tonsillitis. Bursitis of the left shoulder with calcification occurred in 1937. Her family history was irrelevant. On January 1, 1940, an uneventful labor had terminated in the delivery of a normal child. There had since been a small increase in weight, which at the time of consultation was slightly above the estimated normal.

Physical examination revealed an alert, young white female of healthy appearance, with normal gait and posture. Height, 61 inches; weight, 135 pounds; temperature, 100° F.; pulse, 90; blood pressure, 126 mm. Hg systolic and 84 mm. diastolic. Pupils were equal, moderately contracted, and reacted to light and during accommodation. Sclerae were clear, and extrinsic movements normal. There was no strabismus and no exophthalmos. Ears were normal. Nasal mucosa was reddened and congested, with a thin mucopurulent discharge. Teeth and gums were normal, and tongue clean. Tonsils were grossly infected, and the pharynx was reddened. The thyroid gland was not enlarged. A few cervical lymphatic glands were palpable. The breasts were of equal size and exhibited no masses or tenderness. Cardiac sounds were normal in intensity, quality, and rhythm, without adventitious sounds. Lungs were clear. Examination of the abdomen proved negative with the patient in the recumbent position. On sitting and standing, the smooth, round lower pole of a mass, which was firm and insensitive to pressure, was palpable in the right upper abdomen just above the level of the umbilicus. The pelvis was within the normal range. Urinalysis and hemogram were negative. Icterus index was 9, basal metabolic rate, — 6. Fluoroscopic examination of the chest proved negative. Roentgenographic studies of the gastrointestinal tract and of the gall-bladder (Graham-Cole technic) disclosed no abnormalities. An intravenous pyelogram revealed nothing abnormal. A radiograph of the nasal accessory sinuses showed slight clouding of maxillary sinuses and anterior ethmoids.

All radiographs of the abdomen revealed a mass which occupied the right upper quadrant. Its inferior pole was rounded, but in nowise resembled the lower border of the liver. It was impossible to determine from the films whether the image represented a prolongation of the liver or a separate mass. The patient was referred to Dr. H. H. Kerr of Washington, D. C., for exploratory laparotomy.

On August 5, 1940, under anesthesia with avertin and nitrous oxide, a high right transverse incision was made from above the costal border in the axillary line to the midline above the umbilicus. The fascia of the external oblique muscle was

split in the direction of its fibers, and this incision was carried across the anterior sheath of the rectus. The internal oblique and transversalis muscles were likewise split in the direction of their fibers, and the juncture of these two incisions was carried across the posterior sheath of the rectus. The rectus muscle was withdrawn and the peritoneum was opened in a transverse direction. The gall-bladder presented a normal aspect, but to its right there projected from the inferior surface of an apparently normal liver a firm nodular tumor the approximate size of a large orange. The gall-bladder was slightly adherent to the left side of the tumor and was dissected from the latter above the line of cleavage, which could be followed backward into the substance of the liver, thus permitting the tumor to be shelled out intact with only moderate loss of blood. Bleeding from the substance of the liver was controlled by electric coagulation, and the raw area of the under surface of the liver was almost completely closed by a tranverse suture of plain catgut. The abdomen was closed with chromic catgut in the muscular layers and with silkworm gut in the skin. No drains were inserted. Convalescence was uneventful.

At operation the liver appeared entirely normal, and in particular exhibited absolutely no evidence of cirrhosis or other pathological phenomena related to the possible origin of the tumor. Macroscopically the round tumor presented a roughly nodular external aspect and measured about three inches in diameter.

Microscopic examination of a section of the tumor revealed hepatic parenchyma which was divided into unequal lobules by hyperplastic interstitial fibrosis and bile channels, and advanced interstitial fibrosis in the portal areas, with numerous lymphocytes and an occasional leukocyte which indicated a process that was still active. The bile ducts were hyperplastic and in certain areas approximated neoplastic activity, although the cells were regular and polarization normal.

Diagnosis: Liver tissue exhibiting portal cirrhosis with active hepatitis and hyperplasia of bile ducts.

This picture presented, therefore, an encapsulated tumor mass readily shelled off from the inferior surface of the liver, which on section was found to exhibit all the usual characteristics of liver tissue involved in an active cirrhotic process. At the same time the parent organ appeared grossly normal and the patient free from all clinical evidence of disease. In effect, the mass was a histoid tumor that was the seat of focal cirrhosis, but without signs of malignancy, i.e., a benign hepatoma.

In the face of the above facts the etiology must remain, for the present at least, obscure. It is, of course, not clear whether this mass arose from a congenital cell-rest which later developed inflammatory activity, or whether an area of focal cirrhosis became localized as an extra-hepatic tumor. The well marked encapsulation of the mass and the individual's apparent freedom from symptoms might point to the former origin. On the other hand, descriptions of previously recorded cases would tend to support the latter view. Nevertheless, none of the cases reviewed exhibited this association of apparently normal tissue in the parent organ with an active pathological process in the histoid tumor.

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THE VANISHING LUNG; REPORT OF A CASE OF ADVANCED BULLOUS EMPHYSEMA *

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THE title of this paper is not original. Burke,[1] in 1937, first used the term in reporting the case of a white man of 28 with advanced bullous emphysema whom he had followed for five years and who finally died and came to autopsy. Serial roentgenograms in this case revealed the progressive increase in size of these bullae until, just before his death, there was little remaining lung substance. Burke, in reporting the case, stated that it was one of the most advanced cases of bullous emphysema on record. I studied the prints from the roentgenograms of this case and feel that the case I shall report to you in this paper, in so far as roentgenographic evidence of advancement is concerned, is more advanced than his.

Pulmonary emphysema may be defined as a condition of the lungs brought about by over-distention of alveolar walls with a resultant loss of their elasticity and finally their rupture.

Christie[2] has subdivided pulmonary emphysema into four types: (1) Chronic obstructive or hypertrophic emphysema; (2) senile or atropic emphysema; (3) acute vesicular emphysema; and (4) localized or compensatory emphysema.

It is not within the province of this paper to discuss these various forms in detail. As a matter of opinion I am not convinced that any of these forms, with the exception of chronic obstructive emphysema, are clinically important. Senile emphysema is not so much a condition of the lungs as it is of the chest wall. Best and Taylor[3] advance the theory that this is a postural emphysema. A degeneration of the vertebral discs of the thoracic vertebrae takes place in these old people causing kyphosis of the thoracic spine. The anteroposterior diameter of the chest becomes larger, and the lungs enlarge to fill the larger thoracic space. There is little reduction in the vital capacity, little change in the oxygen saturation of the blood, and few symptoms in these cases.

Acute pulmonary emphysema has been observed in mountain climbers both in the Alps and the Andes, and as the condition has appeared to be temporary, there being no permanent emphysema resulting, it would appear that we may dismiss this form of emphysema as being of little more than academic interest.

Compensatory emphysema has been the term applied to hypertrophy of a lung when the contralateral lung or a part of a lung has been thrown out of

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function by a pneumothorax, by thoracoplasty, or by atelectasis. If this is true emphysema at all it is probably not of great clinical importance.

Chronic obstructive emphysema is the type of pulmonary emphysema in which we are interested because this is the clinically important form and the cause of the vanishing lung. It seems wise to discuss the present conception of this treacherous and insidious disease, for its incidence is high, its crippling effects on those it strikes considerable and often most distressing. What then is the etiology of chronic obstructive emphysema? Many theories have been advanced to explain it. For years we have heard that glass blowing and the blowing of wind instruments have been important causes. Laennec was the earliest proponent of this theory which came down through the ages with no more proof to substantiate it than the statement of its originator. Christie [4] did much to disprove this theory. He made a careful study of the literature and quoted the reports of many investigators who had examined large numbers of players of wind instruments in bands and just as many glass blowers and who had found almost no cases of clinical emphysema among them. In fact, Christie found only one observer who could produce any evidence in favor of the theory that glass blowing and the blowing of wind instruments produced the disease. This was Matussewitsch (1934), a worker in the Leningrad Institute for the Study of Occupational Diseases. Christie found many discrepancies in Matussewitsch's report and was of the opinion that it could not withstand careful analysis.

It appears that there is only one theory that does withstand careful analysis and that is the theory of chronic alveolar strain plus partial bronchial obstruction. It is a conceded fact that the vast majority of patients with pulmonary emphysema have been afflicted with some chronic lung complaint, such as asthma, chronic bronchitis, bronchiectasis, pulmonary tuberculosis, silicosis, or possibly bronchiogenic carcinoma. In other words they have been subject to persistent cough for long periods. Cough alone, however, is apparently not enough. The mechanism responsible appears to be the repeated insults to the alveolar walls brought about by repeated sudden increases of intra-bronchiolar and intra-alveolar pressure during the act of coughing, with the additional important factor of the partial obstruction of these bronchioles owing to the presence of mucus and to scarring from fibrosis and pulmonary arteriolar sclerosis. This obstruction is often of such a nature that, valve-like, air can get through on inspiration but on expiration, as the bronchioles contract, air cannot get out but is trapped within the alveoli distending them. This happens so often and the alveolar walls are in such a state of over-distention that finally the elastic fibers undergo degeneration and the alveolar walls lose their elasticity. After elasticity has been lost further stretching may cause the alveoli to rupture. When this happens several things may occur. If the alveoli so stretched are near the surface of the lung the air liberated when they rupture may separate the pleura from the underlying alveoli, and a blister or emphysematous bleb form on the surface of the lung. Later, due to some sudden exertion or strain on the part of the individual so affected, this bleb may rupture allowing air to get into the pleural cavity, thus causing a spontaneous pneumothorax. If the alveoli so affected are considerably below the surface of the lung they may rupture into other alveoli, and by coalescence a cavity may form within the lung

with the formation of a bulla. These emphysematous bullae are connected by small openings with the bronchioles, for gas samples have been taken from them and upon analysis have shown atmospheric air.

Miller [5] in 1926 was the first to make the distinction between blebs and bullae. Miller cut open these emphysematous sacs in the lungs of those who had died

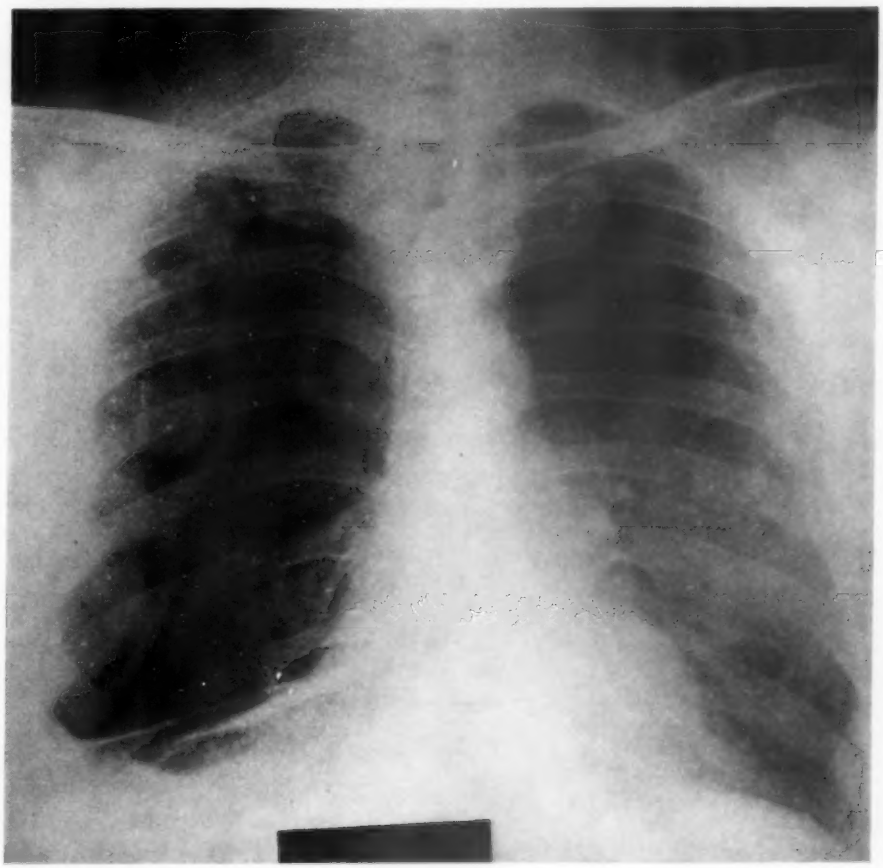

FIG. 1. Postero-anterior plate showing complete absence of lung markings in the entire right hemithorax except for a cobweb-like fibrosis at the extreme base. There is absence of markings in the upper half of the left lung field with increased markings in the lower half of this lung. There is no mediastinal shift, no enlargement of the heart, and no evidence of collapsed lung margin.

and studied histological sections of them. He was convinced that the condition of the alveoli surrounding a bulla differed from that of a bleb in that in the case of the bulla the adjacent alveoli were distended, whereas the alveoli beneath a bleb were compressed.

Miller's [5, 6] conception of a bleb is that it is a thin walled bladder-like prominence on the surface of the lung caused by air from ruptured alveoli near the surface of the lung pushing the pleura out and separating it from the underlying alveolar walls. A bulla, on the other hand, is a collection of air formed by

vesicular emphysema and contained within the lung, and though it often projects beyond the surface of the lung it is covered by intact pleura. This distinction may appear to be a rather fine one. Some observers use the terms synonymously. Much remains to be done in the fields of pathology, histology, and physiological chemistry before the true conception of emphysema and its physical manifestations can be confidently stated.

Christie [2] has pointed out that overstretching and rupture of the lung alveoli are most apt to occur where the lung is least supported, namely at the apex and along the lung margins. He likewise explains the typical barrel-chest conformation of the emphysematous thorax as due to the loss of the elastic pull of the lung when its elasticity disappears, the chest thus assuming permanently the shape it normally assumes only in deep inspiration. This increase in volume of the thorax tends to impair function. The elasticity being lost the lung is unable to deflate by the normal passive process of elastic recoil, and it becomes necessary for the accessory muscles of respiration to squeeze the air out of this failing lung. Expiration becomes prolonged. There is a reduction in total as well as vital capacity, with an increase in residual air.

The chief symptoms of patients with pulmonary emphysema are dyspnea and cough. Kaltreider and Fray [7] believe the dyspnea can be explained by the mechanical impairment of the respiratory bellows. The sharp rebound of the normal lung occurring at the end of inspiration is an important mechanical factor in the efficient ventilation of the alveoli. It is lost in the emphysematous lung, resulting probably in a slower diffusion and thereby faulty aeration of the blood. The cough, according to Christie,[2] is due to bronchial irritability and to chronic bronchitis with which these patients are afflicted. The plum-colored cyanosis, so common in emphysematous individuals, may be partly explained by a compensatory polycythemia and partly by a carbon dioxide retention in the blood.

Dyspnea becomes more and more troublesome and finally oxygen must be resorted to periodically. Many patients succumb to pneumonia while others die of heart failure. A few succumb to the accident of spontaneous pneumothorax.

The diagnosis of chronic obstructive emphysema is chiefly roentgenographic. We have been well aware of the presence of emphysema by the brilliant areas of rarification in which no lung markings could be seen. The significance of fine hairline curved and annular shadows in the films adjacent to these areas of rarification, however, has been missed or misinterpreted by many observers in the past. Some have considered them as tuberculous cavities whereas others have believed them to be localized pneumothorax pockets. Miller [8] in 1933 reported the case of a negro laborer of 66 who had pulmonary tuberculosis and in whose lung a large emphysematous bulla had been mistaken for a tuberculous cavity. Repeated sputum analyses in this case had been negative for tubercle bacilli, and only at autopsy was the real nature of the cavity ascertained. This is not an uncommon mistake. It has probably sent more than one non-tuberculous patient to a sanatorium.

Friedman [9] considers these annular shadows to be zones of atelectasis in the alveoli adjacent to blebs and bullae caused by compression and to substantiate this quotes the earlier work of Laurell,[10] who, he states, was the first to prove experimentally that blebs and bullae cast ring-shaped shadows on the roentgenogram. Friedman further states that blebs and bullae are occasionally found in the lung in the absence of generalized emphysema.

The gross pathology of chronic obstructive emphysema is interesting. The lung is voluminous and, as Richards[11] brings out, has a pale gray instead of a normal pink surface. In Burke's advanced case when the chest was opened the lungs ballooned out and spilled over the chest cavity as under pressure. Emphysematous lung does not crepitate, but pits on pressure. Histologically there is a pulmonary arteriolar sclerosis and increase in the connective tissue. The

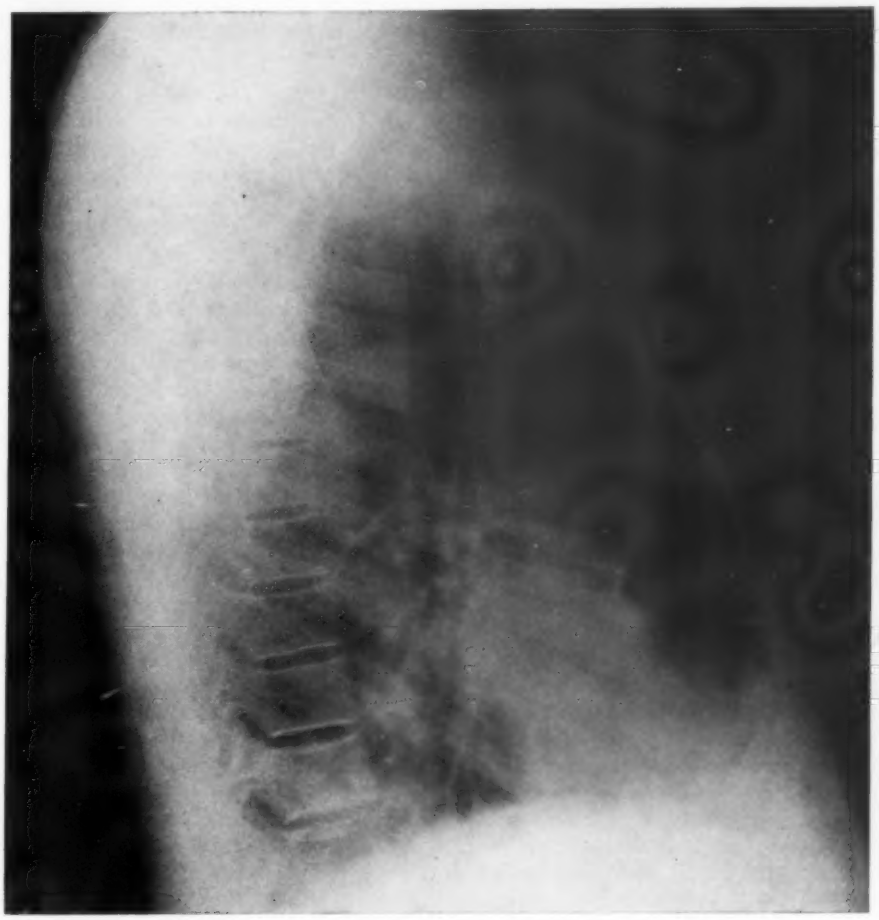

FIG. 2. Lateral plate in which no lung markings are apparent except at the extreme base. No evidence of mediastinal tumor is seen.

bullae, seen within the lung substance, usually connect with bronchioles although in some cases even on most careful examination no such openings could be found.

The prognosis of chronic obstructive emphysema is not good. Recovery is out of the question. The process spreads and as bullae increase in size good lung tissue becomes either compressed or over distended until less and less lung remains. In Burke's case practically nothing was left in the left chest cavity but a giant bulla occupying four-fifths of the space. There were only a few fibrous septal strands at the base of the left lung.

In the treatment of these cases it should be emphasized that in advanced cases relief is only temporary. In all cases, early and advanced, the patient with emphysema should be protected as much as possible from acute respiratory infections which would certainly aggravate his chronic condition. Life in a dry warm climate at an altitude below 3000 feet would be the ideal. No excessive muscular strain such as heavy lifting or strenuous exercise should be allowed, not only because this would add to the burden of an already overstrained circulation but also because it might bring about, from sudden rupture of emphysematous tissue, the dangerous accident of spontaneous pneumothorax. The patient should live his life at a slower tempo and develop a philosophy of life which will enable him to do so and still be happy. Unfortunately the economic angle enters the picture here, as it does in most chronic illnesses, and the man with advanced emphysema who must work hard for a living is indeed to be pitied.

Case Report

S. P. F., a white American male of 41, was first seen by me at his residence on the night of January 24, 1940. He complained of having had a very severe chest cold for two days, with a cough so distressing that the preceding night he had been unable to sleep because of it. There had been no chill, no frank hemoptysis, no blood-tinged or prune-juice colored sputum, in fact very little sputum at all. There was slight chest pain on coughing but not on inspiration. There was considerable dyspnea during and after a coughing spell, and the cyanosis which was slight at rest was intensified and plum-colored during these coughing attacks. The patient stated that for some months, perhaps for a year or more, he had noticed increased breathlessness on exertion and likewise that he was unable to sleep on the left side without coughing and becoming breathless. The significance of this last symptom was not clear at the time, but became so later.

The past history revealed that the patient had had epilepsy from early childhood, with grand and petit mal at infrequent intervals. He had had no attacks for nearly a year and one or two attacks a year had been about his limit. He had had diphtheria and acute nephritis in early childhood and pneumonia twice before he was 10. At the age of 11 he had had acute rheumatic fever following which he had no symptoms referable to his heart, and apparently no one had ever detected any signs of mitral or aortic valvular disease. He had none at the time of examination, at any rate. While at school and college he had played class hockey and other less strenuous sports without any abnormal symptoms appearing. There is only one clue as to the duration of the disease with which he is afflicted. While at college in 1917 a routine physical examination upon admission revealed his chest expansion to be four inches. Two weeks before his recent acute respiratory infection, in early January of 1940, he had gone to a certain New York gymnasium for "conditioning" and when examined there his chest expansion was nil. In spite of this he was permitted to take the strenuous "conditioning" exercises and could not understand why it took him so long to recover from the dyspnea brought on by them. No one else taking the course appeared to be bothered this way. It puzzled him, but he explained it as no doubt being due to the fact that he was "out of condition" and overweight. His weight in college had been 140, his present weight 190.

Upon physical examination the patient appeared slightly cyanotic, dyspneic, and overweight. His height was 5 feet 11 inches, his weight 190 pounds. His pupils reacted well. His teeth were false. He had a history of many abscessed teeth. His heart sounds were somewhat distant but otherwise of good quality. No murmurs could be heard. His chest, a broad heavy one and not a typical "barrel chest,"

was resonant throughout. The breath sounds, except at the left base, were absent, and many sibilant and sonorous râles were heard from about the level of the fourth thoracic spine on the left to the extreme base. No signs were heard on the right. The true significance of these signs was not appreciated at the time. The remainder of the physical examination was negative except for a blood pressure of 180 mm. Hg systolic and 80 mm. diastolic. The temperature by mouth was normal, the pulse rate 90.

I felt that the patient had an acute bronchitis, but that in view of his general appearance, the rather unusual chest signs, and the elevated blood pressure it would be wise to have him admitted to the hospital for careful study. He was given codeine for the control of his cough during the night and the following morning was admitted to Scrymser House, St. Luke's Hospital.

Laboratory tests of the patient were as follows:

Urine—clear, acid, 1.024, very faint trace of albumin, no sugar. Microscopically no casts, pus, or red blood cells were seen.

Blood Kline test was negative. Blood count: hemoglobin 105 per cent (15.3 grams); red cells 5,000,000; white cells 12,500; polymorphonuclear leukocytes 78 per cent, lymphocytes 18 per cent, monocytes 3 per cent, eosinophiles 1 per cent. There was a slight shift to the left. The red cells were normal in appearance.

Blood urea nitrogen 9.8 mg. per 100 c.c. Fasting blood sugar 143.0 mg. per 100 c.c. Blood cholesterol 180 mg. per 100 c.c. Blood chlorides 5.0 per cent.

The electrocardiogram showed normal sinus rhythm, right axis deviation, auricular and ventricular rate 70, slightly low voltage, PR interval time 0.19 sec., QRS complex 0.08 sec., notched P-waves in all leads, T-waves upright in all leads, Lead IV CF normal.

Stereoscopic roentgenograms of the chest revealed an absence of lung markings in the entire right hemothorax except for a few fibrotic cobweb-like strands at the extreme base. The upper half of the left lung field, corresponding to the left upper lobe, revealed the brilliancy characteristic of the absence of lung tissue, whereas the lower half of the left lung field, corresponding to the left lower lobe, showed increased markings.

Fluoroscopic examination of the chest revealed a normal although somewhat diminished excursion of the diaphragms, the right having an excursion of approximately an inch, the left approximately two inches. Upon inspection in the oblique and lateral views no evidence of tumor mass could be seen in the mediastinum. The heart was not enlarged.

The evidence produced by the roentgenograms came as a complete surprise. This patient had been seen by six or eight physicians in a period of 20 years and no chest roentgen-rays had been taken prior to this, in spite of the fact that in 1936 he had been carefully studied in a large medical center in which gastrointestinal roentgenographic series, blood studies, basal metabolism, and other tests were made.

Looking at the case in retrospect it became clear why dyspnea on exertion was becoming more pronounced as time went by. It also explained the patient's discomfort while lying on the left side at night. By so doing he would splint the only part of the lung which was functioning and having no lung capacity on the right he naturally became cyanotic and dyspneic.

It was impossible to date exactly the beginning of this disease. The fact that the patient's chest expansion at college in 1917 had been four inches suggests that it did not date back to that period. At least, if he did have emphysema at that time it must have been slight.

The etiology of this case is probably that of most cases of emphysema. There are many theories, none of which can be proved. It is true that this patient had numerous respiratory infections, including pneumonia twice, in early childhood. Likewise he had been a very heavy smoker all of his adult life and had had what he

termed a cigarette cough for years. It is quite probable that excessive wear and tear on the alveolar walls caused by cough and partial obstruction of the bronchioles by mucus were the causative factors in this patient's case. The possibility of aspiration during one or more of his grand mal seizures has been considered but discarded as unlikely.

As soon as the roentgenograms of the chest had been seen it seemed obvious that we were dealing with bullous emphysema. The only other possibilities to consider were spontaneous pneumothorax and the "balloon cysts" of congenital cystic disease. If it were the former the patient should have had severe symptoms at the onset of the accident. He did not. Likewise, the lack of mediastinal shift and the bilateral involvement are factors which would rule against spontaneous pneumothorax. Also the border of the collapsed lung should be well defined in cases of spontaneous pneumothorax. As to congenital cystic disease, a rare condition at any age, it is extremely rare at 41, although Wood [12] reported a case in a man of 43. The fact that symptoms in this patient were relatively recent and the fact that he remembered that his chest expansion in college in 1917 was four inches are against the condition's having existed at that time.

The functional power of the remaining lung tissue was studied by Dr. Dickinson, W. Richards, Jr., and Dr. André Cournand. The results of these tests were as follows:

Lung Volumes	Before Vaponephrin	After Vaponephrin
Vital capacity in liters	2.378	2.572
Residual air in liters	3.447	
$\frac{\text{Residual air} \times 100}{\text{Total lung volume}}$	59.2%	
Maximum breathing capacity in liter/minutes	32.2	47.2

Rate of Oxygen Removal per Liter of Ventilation in c.c.

At Rest	During Exercise
41.0 (normal—47 c.c.)	45.8 (normal increase 6–7 c.c.)

Arterial Blood Oxygen Hemoglobin Saturation

At Rest	After Exercise
94.2	94.5

Status of Circulation during Infusion Test

	At Start	At End
Venous pressure (mm. H_2O)	85	120
Circulation time sec.	14	
Vital capacity in liters	2.205	2.230

These studies revealed a remarkable functioning power of the remaining lung tissue, more than we had hoped for.

Treatment presents a difficult problem. Croswell and King (1933) [13] reported the case of a boy of two and a half years who had a large "balloon cyst" in his lung, into which they had injected, through the chest wall, iodized poppy seed oil. They believed that a bronchus opened into the cyst and that if they could obliterate this opening the air in the cyst would absorb and the atelectatic lung reëxpand. They turned the child over in various positions so that the oil would come in contact with all of the cyst wall. A serous exudate formed, the opening evidentally was sealed off, and the lung reëxpanded as they had hoped. This patient was well at the end of two years' observation. Wood [12] criticized this procedure, stating that it was not

without risk to the patient. It seemed to Dr. James Alexander Miller, with whom I consulted in the case, and to me that such a procedure with our patient would be dangerous and unwise. The fact that the affair was bilateral increased the risk, and we felt that inserting a needle through the chest wall into the bullous cavity might bring about sudden spontaneous pneumothorax with the death of the patient.

In view of the results of the functional lung studies it seemed possible that the patient with proper care might live for several years, even perhaps many years, in reasonable comfort. It was decided that he should move to Tucson, Arizona, for the winter and spring months to insure clear, dry air, with the hope that this might lessen the likelihood of respiratory infections. He was instructed to avoid strenuous exercise and heavy lifting, and was cautioned about smoking and the use of alcohol, as the former would act as an additional bronchial irritant and the latter would elevate his pulse rate and add to the load of an already overburdened circulation as well as lower his resistance. This man has been a very heavy smoker for 20 years or more which may be a factor in causing this condition. A diet which was sufficient to maintain good health but which would not increase his weight was prescribed. As the patient was overweight it was felt that it was wise for him to reduce considerably. The diet was low in fats and carbohydrates but high in protein, vegetables, fruits and vitamins. He was advised to use an abdominal belt which increases intraabdominal pressure and thus elevates the diaphragm and increases the vital capacity. Alexander and Kountz [14] devised such a belt in 1934 and in 25 cases found that it increased vital capacity 39 per cent. As the patient is in a position to carry out these directions, such hopes for his future seem within the realm of probable achievement.

Summary and Conclusions

1. Chronic obstructive emphysema is an insidious disease of the lungs in which the elasticity of the alveolar walls is lost, with the result that these walls rupture.

2. When the air from the ruptured alveoli is contained within the lung itself and covered by intact pleura the resulting cavity is known as a bulla and this type emphysema is bullous emphysema.

3. The probable cause of emphysema is not glass-blowing or the blowing of wind instruments but, it seems reasonable to assume, the wear and tear on alveolar walls due to sudden and frequent increases in intraalveolar pressure during the act of coughing in patients afflicted with asthma, chronic bronchitis or some other pulmonary disease of chronic character. The added factors of mucous obstruction in the bronchioles, and fibrous scarring and arteriolar sclerosis are likewise of considerable importance in the etiology.

4. A case of far advanced bullous emphysema with good functioning power of the remaining lung tissue is reported.

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A CASE OF PANCREATIC LITHIASIS *

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ALTHOUGH some 113 or more cases of pancreatic lithiasis have been reported, it is still rarely diagnosed during life. In 1937 Höchstetter [1] was able to find only four cases diagnosed by roentgen-ray before operation and 30 diagnosed on the operating table. The rest of the reported cases have been revealed only at autopsy. Since the symptoms produced are variable and quite unreliable, and since the stones found in the pancreas are ray-opaque, the roentgen-ray is our most valuable means of diagnosis in this condition. As was pointed out by one of us (D. B. F.) in 1935,[2] it is necessary to rule out other abnormal opacities found in the abdomen. A cholecystogram will aid in ruling out gall-stones and a pyelogram in ruling out kidney stones. As a further aid in ruling out these conditions and calcified retroperitoneal or mesenteric lymph nodes, fluoroscopy and films taken in the lateral and oblique positions should be used. Pancreatic disease is to be suspected if in the gastrointestinal series there is a deformity and elongation of the duodenal arc.

CASE REPORT

W. D., a colored male, 45 years old, a huckster by occupation, gave a history of repeated hospitalization for "stomach trouble" since 1918. The records of this hospital † revealed seven previous admissions in which abdominal distress and a chronic cough were the chief complaints. The chest trouble was described as a chronic, productive cough with occasional pains in various parts of the chest. The gastrointestinal symptoms consisted of constant, dull, epigastric pain with periodic attacks of rather

* Received for publication November 14, 1939.
† Walter Reed General Hospital, Washington, D. C.

FIG. 2.

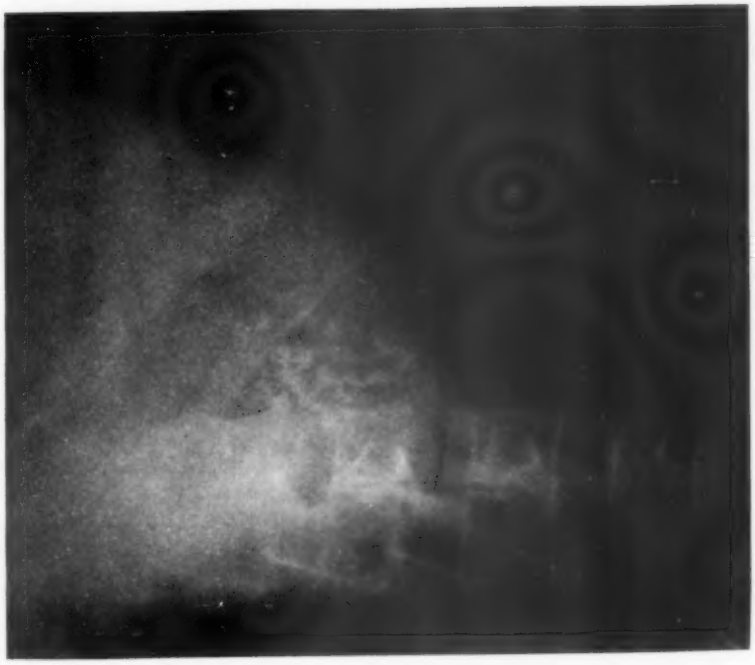

FIG. 1.

severe epigastric pain, constipation, intolerance to coarse foods, loss of about 30 pounds in weight, weakness and occasional vomiting. He maintained that the symptoms had persisted, unchanged as to severity, since 1918. About one year previously he had noted a moderate jaundice which lasted for about eight months, but during this time there was no change in the character or severity of his other symptoms. At the time of his last admission, approximately six years previously, he had complained of a dull aching and dragging pain in the epigastrium, radiating to the hypochondrium bilaterally, not related to ingestion of food.

Physical examination revealed a poorly nourished male weighing 112 pounds, with a few inconstant coarse râles in both lungs, moderate enlargement of the liver, moderate tenderness over the gall-bladder on deep palpation, associated with some muscular resistance in this region. Many teeth were missing and there was a moderate kyphosis.

Tentative diagnoses of chronic bronchitis, chronic gastritis and cirrhosis of the liver were made.

Before completion of the studies it was noted that while in the hospital he was subject to irregular attacks of acute epigastric pain not related to food or to evacuation of the bowel, and not relieved by alkaline powders or by enemata. Between attacks he was quite cheerful, but during the attacks his facial expression was one of intense pain. At times he would bend sharply forward grasping the epigastrium with both hands, and at other times he would lean over the bed and groan. Muscle guard was a constant finding in the upper abdomen, but during the attacks there was true rigidity.

The survey revealed moderate cloudiness of both maxillary sinuses, a poorly functioning gall-bladder, a bizarre but rather constant deformity of the duodenal bulb and a normal barium enema. It was on the films of the gastrointestinal series that a solitary calcified nodule in the liver, as well as fine and medium-sized calcified areas in the region of the pancreas, were first noted. Later films of the abdomen including lateral and oblique views fixed the position of the multiple, small calcified areas as being in the pancreas. Urine, feces, sputum and blood examinations were all essentially normal. Blood Wassermann and Kahn, gastric fractional analysis, blood sugar, bromsulphalein, glucose tolerance, electrocardiogram, roentgen-ray of the chest and proctoscopic examination were all within the normal range. The icterus index was 10.

Careful observation on the ward later disclosed that the attacks of epigastric pain were definitely related to meals in that even the smell or the sight of food would induce the pain. It was further noted that if he ate rapidly he could sometimes eat most of his tray before the onset of acute pain. Because of the associated gall-bladder disease and the severity of the attacks, surgery was advised, but it was refused and the patient was discharged from the hospital unimproved, with a diagnosis of pancreatic lithiasis based on clinical and roentgen-ray findings.

About 18 months later he had an attack of agonizing pain which caused him to writhe on the floor and he was re-admitted to this hospital. Examination revealed extreme tenderness associated with moderate rigidity and rebound tenderness in the midepigastrium. He readily consented to operation. On exploration gall-bladder adhesions were released. The gall-bladder was otherwise normal. The pancreas was enlarged to about five times the normal size, indurated, and so distended that the usual lobulated appearance was obliterated. The surgeon was unable safely to expose the head of the pancreas except posterior to the first portion of the duodenum. At this point the pancreas was incised and one small, very white calculus removed. Many calculi in the terminal ducts could not be removed. Biopsy showed no malignancy. The convalescence was smooth. The patient's appetite improved and he gained over 20 pounds in six weeks. About 10 weeks after operation there was a sudden return

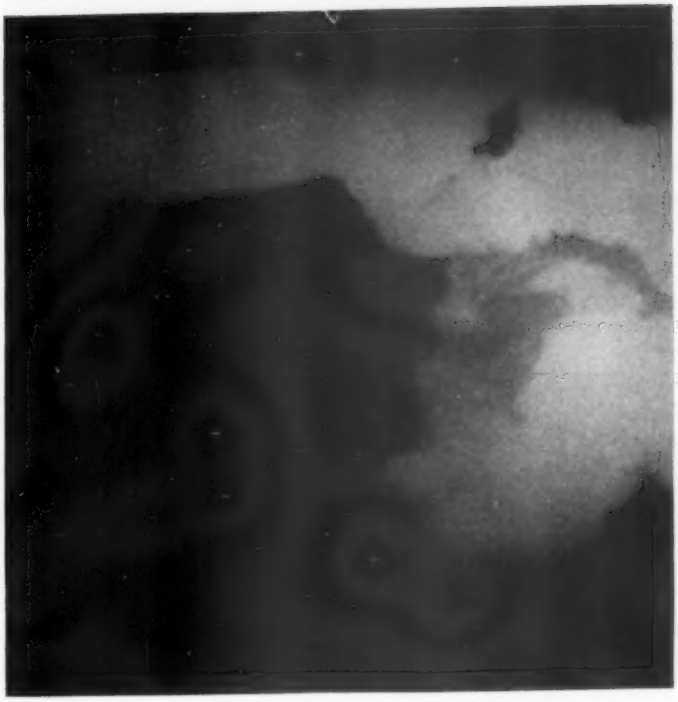

FIG. 4.

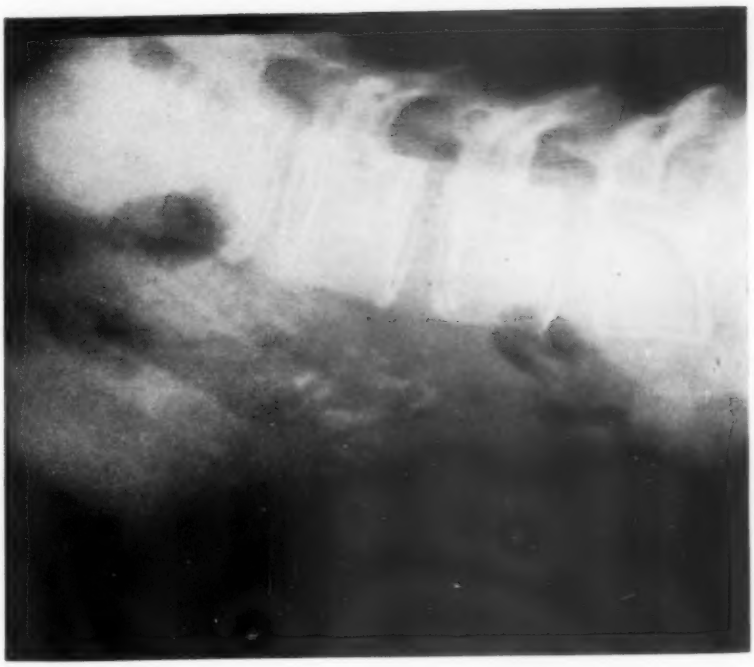

FIG. 3.

of his pain which we attributed to a blocking of the main pancreatic duct with another stone. We do not believe that when the stones are distributed as they are in this case there is any hope for permanent cure, but will recommend another trial at surgery.

This case presented no exception in the elusiveness and inconstancy of the symptoms and findings during prolonged and repeated examinations. The most common and constant symptom in this case was epigastric pain, not related to meals at first but later caused by the sight or smell of food.

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EDITORIAL

THE FEMALE HORMONES

BECAUSE there is still much misapprehension as to the conditions in which these hormones are effective and as to their limitations, a brief authoritative discussion of the available pertinent facts concerning them seems desirable. The following summary has been prepared by Dr. Elmer L. Sevringhaus * and is published as an editorial in order to help toward a clearer understanding and more intelligent use of these preparations.

The hormones which are distinctively female are the estrogens and progesterone. The first group includes estradiol (the most potent), estrone (next in potency but more commonly known and used), and estriol (still less potent). There are also a large number of similar compounds which are of biological significance in limited situations but of little importance to the clinician. The synthetic estrogen, stilbestrol, must be kept in mind from a therapeutic point of view. Progesterone, product of the corpus luteum, is unique and there are no similar naturally occurring compounds of significance.

Physically these compounds are all solid, waxy materials, called steroids, which are very poorly soluble in water but more soluble in alcohol and oils. The water solubility of estrone is 2 mg. per liter, or 20 international units per c.c., which is somewhat greater than the highest concentrations of the hormone found in any tissues or body fluids. For therapeutic purposes the greater solubility in oils, above 10,000 international units per c.c., is of real importance. Perhaps this solubility in oils has something to do with the distortions of reproductive function which occur in obesity and which are often relieved by weight reduction alone.

Chemically these hormones are closely related, as derivatives of a rather complicated polycyclic compound, pregnane. The same statement applies to the male hormone, testosterone, to the hormone molecules derived from the adrenal cortex, and to a number of other biologically active substances, some in the field of food materials, others of drugs. The chemical tests for identification of any one of these compounds are involved, and the color reactions are usually not specific enough for identification of any one as distinct from another. The assay by means of biological reactions is similarly specific only in the sense of identifying a compound which is purified from the others of similar activity so that its activity per mg. can be determined. In

* Summary of a lecture delivered before the American College of Physicians, April 22, 1942, at St. Paul, Minnesota.

For further details regarding these hormones, readers are referred to: (1) ALLEN, E., DANFORTH, C. H., and DOISY, E. A.: Sex and internal secretions, second edition, 1939, Williams and Wilkins, Baltimore; and (2) Glandular physiology and therapy, second edition, 1942, American Medical Association, Chicago.

the body estradiol is most active, it is easily changed to estrone, probably in the liver, and then to estriol. Only these latter two compounds occur in significant amounts in the urine, and then only somewhat less than 10 per cent of the original material is so found. The fate of the rest of the estradiol is still unknown. Progesterone is converted in the body to pregnandiol, which is then conjugated largely with glycuronic acid, for urinary excretion. Even this process cares for only an uncertain although large fraction of the progesterone. Other metabolic products of progesterone have not been identified.

The sources of all these ovarian hormones include the ovaries, and during pregnancy the chorionic tissues as well. Estrogens appear to come from all parts of the ovaries, the progesterone probably from the transformed luteal cells only. The quantitative aspects of this secretion are known in only the roughest way, owing to the lability of the compounds, the lack of knowledge of all end products, and the unmet need for specific methods for determining any one of the estrogens in the presence of the others.

Estrogens as a group are stimulants of tissue growth, with effects most marked in the myometrium, endometrium, vaginal epithelium, and mammary ducts. The other activities include stimulation of rhythmic contractions in the uterus and Fallopian tubes, relaxation of the muscles in blood vessels, the stimulation of the secondary sex characters, and a reflex activity upon the anterior pituitary. This latter effect is a composite of stimulation of the pituitary by brief application of moderate amounts, and inhibition of pituitary function by sustained exposure to large amounts of estrogen. The variations in the amounts of pituitary and estrogenic hormones are thought to be fundamental factors in the control of rhythmic action of the ovaries. The quantitative laws cannot yet be formulated.

Progesterone induces relaxation of myometrial contractions, reduces the sensitivity of the uterus to posterior pituitary hormone, interrupts the effect of sustained estrogenic secretion on the uterus, but most important of all progesterone induces the transformation of endometrial glands from the type known as proliferative to that called progestational (secretory for mucin, glycogen, and possibly fat). Progesterone is also the stimulant to development of mammary acini preparatory to lactation.

Diagnostic procedures are directed to identify the presence of these two types of hormone, and to determine the amounts active. Histories of patients will show the presence of estrogens, but nothing short of pregnancy will prove progesterone. Tissues obtained by biopsy or curette from the endometrium will show estrogens or progesterone, and will give a roughly quantitative measure of the activity. Microscopic study of vaginal cells, obtained by smear technic, furnishes a better quantitative gauge of estrogens, but so far it tells nothing about progesterone. Urinary examination for pregnandiol is a chemical check on progesterone with quantitative significance of fair reliability. The use of assays of blood and urine for these

hormones, by either biological or color tests, is still a fascinating problem for use in investigative clinics alone.

Therapeutic uses of estrogen include (1) stimulation of development in cases with infantilism, amenorrhea, or hypoplasia of the genitalia or breasts. This use is questionable, for it is prone to leave the ovaries less active than before, certainly not more active and able to carry on reproductive function. (2) Relief from dysmenorrhea may occur at times when the cause is a hypoplastic uterus. Such use is not frequently successful. (3) Treatment of sterility by estrogens is empirical, has little evidence to support it, and there may be risks. (4) Rapid maturing of the juvenile or infantile vaginal mucosa induced by estrogens leads to cure of gonorrheal vaginitis when this occurs before puberty. A similar physiological process is utilized in obtaining relief from the distress of senile vaginitis. (5) The chief benefit obtained from estrogenic therapy is relief from the autonomic and psychic symptoms of the climacteric. It is to be prescribed in doses adequate to achieve the relief, without regard to the inhibitory action on the anterior pituitary. Upper limits on dosage are indicated by restoration of bleeding, or uncomfortable stimulation of the breasts or of libido.

Progesterone therapy is helpful in repeated abortion, perhaps also early in threatened abortion. Dosage is still uncertain, but should be 1 mg. or more frequently repeated. Menorrhagia may be interrupted at times by use of progesterone in large doses. At times certain types of amenorrhea may respond to progesterone if the amenorrhea is dependent on a rather steady secretion of estrogens. Use of progesterone in the treatment of painful breast swelling is still being tried out.

The following methods of administering these hormones are available: (1) Oily solutions may be given intramuscularly, employing estrone, estradiol as the propionate, the relatively crude estrogenic substance, stilbestrol and its derivatives, and progesterone. (2) Probably all these might be given by vaginal suppositories, but this is done now only with estrogens in treating vaginitis. (3) Inunction of any of these compounds in oils, ointments, or in alcoholic solution is feasible, and is of real interest in estrogens for climacteric control. (4) Implantation of pellets under the skin for prolonged absorption is interesting, but probably not of permanent importance, since oral use is so easy. (5) Orally estradiol is not an economical form of therapy, but estrone or estrogenic substances may be used in this way profitably. Doses should be divided into one or more portions daily for most efficient use. Stilbestrol owes its great advantage to its low rate of destruction when given orally. The preparation pregneninolone, a synthetic substitute for progesterone, has some possible future as an orally active substance which produces progestational effects. It cannot be evaluated yet.

ELMER L. SEVRINGHAUS.

REVIEWS

Time and the Physician. By LEWELLYS F. BARKER, M.D. 350 pages; 23.5 × 15.5 cm. G. P. Putnam's Sons, New York. 1942. Price, $3.50.

This is the engaging life story of the much honored and travelled physician, Dr. Lewellys F. Barker. Aside from being of value in giving us a picture of the eminent physician himself, the book adds to chronicles of the Medical School and hospital of the Johns Hopkins University. Much of the author's personal philosophy flavors the book throughout. Dr. Barker has been a pioneer in giving proper emphasis to the importance of studying functional nervous disorders in conjunction with the practice of internal medicine.

Physicians as a group, and more particularly those physicians who are or have been associated with the Johns Hopkins Hospital, will find the book an absorbing account of Dr. Barker's own life, as well as an intimate record of the early days of the hospital.

J. E. S.

The Fundamentals of Nutrition. By ESTELLE E. HAWLEY, Ph.D., and ESTHER E. MAURER-MAST, M.D. 477 pages; 25.5 × 16.5 cm. Charles C. Thomas, Springfield, Illinois. 1940. Price, $5.00.

This book should be extremely valuable to physicians and dietitians. It is a clear, concise discussion of nutrition supplemented by convenient, practical tables, charts, ample reference lists and bibliographies.

Section I is a clear explanation of metabolism and modern methods of measuring it. There are tables for calculating surface area and basic metabolic rate, and determining the probability of normality.

Section II deals with the fundamentals of nutrition, discussing briefly but adequately the importance of the various foodstuffs, the method of calculating the energy requirement, the normal diet and some very practical suggestions for planning low cost meals. A long list of references is included at the end of this section, should the reader wish further to investigate the subjects. A similar list of references follows each section.

Section III contains a number of articles on diet therapy written by different physicians. They cover practically every condition in which diet is used as a therapeutic measure, and each article is followed by a summary of the general principles of the dietary treatment.

Section IV on diet planning contains a well constructed table of 100 calorie portions which gives the weight, the grams and calories of protein, fat and carbohydrate, the vitamin content in International Units for all except C which is given in milligrams, and G (B_2) given in S–B Units, the mineral content in grams for eight minerals, the acid or base excess in terms of c.c. normal solution, and uric acid. There are explicit directions for using this table. There is a chapter on the calculation of diets and a table showing equivalents for interchanges in special diets. A table on the potassium content of foods is included in which the foods are divided into 12 groups according to their potassium content. A table on the cholesterol content of foods contains seven groups which should aid in planning diets for gall-bladder disease. There is an excellent summary of adjustments of the normal diet to meet specific therapeutic needs. This table should make the planning of special diets easier for physician, nurse or dietitian. A table on the approximate quantity yield from one pound of common foods should be useful to the person who helps a patient plan a budget diet.

Section V is an appendix which is extremely valuable for the collection of information on food which it contains. There are directions for evaluating the nutri-

tional status of a patient, including an outline for the nutritional history and definite laboratory methods of studying vitamins with lists of equipment needed. A part of the appendix devoted to milk gives the composition of milks of various mammals and standards for grading milk. A discussion of vitamin products includes a summary of costs, potency and dosage which should be extremely valuable to the physician. The appendix includes a number of recipes and food suggestions for special conditions—recipes for the use of glandular meats, for foods without wheat, milk or eggs. There are some special diet instruction sheets and a list of biologic food groups.

This volume is well indexed and should be an excellent aid to the physician who wants a ready reference on nutrition. It is not a large volume, but the information is extremely well chosen and arranged for use.

F. J.

Surgery of the Ambulatory Patient. By L. KRAEER FERGUSON, A.B., M.D., F.A.C.S.; Section on Fractures by LOUIS KAPLAN, A.B., M.D., F.A.C.S. 923 pages; 16 × 23.5 cm. J. B. Lippincott Co., Philadelphia. 1942. Price, $10.00.

Surgery of the Ambulatory Patient succeeds, in large measure, in placing at the disposal of the medical profession a book that gives useful information regarding the ambulatory patient, whether the reader be a general practitioner, a beginner in surgery, or an advanced student in the surgical field. In addition, the undergraduate student in medicine may find many informative chapters between its covers such as those on bandaging, dressings, inflammation, chemotherapy, lymphangitis, etc. The practitioner in other fields may gain valuable information on many subjects such as the eye, ear, hemorrhage from tooth extraction, torticollis, bursitis, painful joints, painful backs and a host of other conditions that cannot easily be picked up in any other single textbook. Many subjects are discussed, however, that, in my opinion, should not be interpreted as ambulatory conditions, and the definitive treatment in numerous cases illustrated should be instituted only while the patient remains for a few days in a general hospital.

T. B. A.

COLLEGE NEWS NOTES

As of July 1, 1942, the following physicians who are Fellows or Associates of the American College of Physicians are on active duty in the armed forces of their country:

Gordon A. Abbott
W. Osler Abbott
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George A. Alden
Edward L. Alexander
Ralph I. Alford
William H. Allen
Stanton T. Allison
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Jere W. Annis
Irving L. Applebaum
Charles P. Archambeault
Harry G. Armstrong
James E. Ash
George F. Aycock
John T. Aydelotte

Theodore L. Badger
George Baehr
Walter H. Baer
Crawford N. Baganz
M. Herbert Barker
Clarke H. Barnacle
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Clarence R. Bell
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John T. Bennett
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Edmund H. Berger
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Edward G. Billings
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Rankin C. Blount
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George W. Calver
Richard B. Capps
A. Albert Carabelli
Arturo Carbonell
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Leon D. Carson
Martin G. Carter
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Frederick Ceres
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Donald T. Chamberlin
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Paul M. Crawford
Neil L. Crone
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Edward B. Vedder
Walter A. Vogelsang

J. Franklin Waddill
Don C. Wakeman
Frank B. Wakeman
Albert W. Wallace
C. Stewart Wallace
Eugene L. Walsh
Arthur B. Walter
Charles H. A. Walton
Robert L. Ware
Otis S. Warr
Leon H. Warren
Richard N. Washburn
Charles E. Watts
Edward T. B. Weidner
Samuel A. Weisman
John M. Welch
Guy W. Wells
Oliver C. Wenger
Winthrop Wetherbee, Jr.
R. James Wharton
Daniel W. Wheeler
Arthur E. White
Edward C. White
Joel J. White
Samuel A. White
T. Preston White
Ely L. Whitehead
Hugh G. Whitehead, Jr.
M. Richard Whitehill
Joseph H. Whiteley
William W. Wickersham
Francis W. F. Wieber
Carl H. Wies
Otis Wildman
Edward A. Wilkerson
John H. Willard
Alton F. Williams
John M. Willis
Frank W. Wilson
George C. Wilson
Paul W. Wilson
Walter J. Wilson, Jr.
Donald J. Wolfram
Sidney E. Wolpaw
John C. Woodland
Thomas D. Woodson

Asher Yaguda
Charles T. Young
Dwight M. Young
Frank W. Young

Edwin E. Ziegler
J. La Monte Zundell

Additions to this list will be published periodically.

New Life Member of the College

Dr. Clayton B. Ethridge, F.A.C.P., Washington, D. C., became a Life Member of the American College of Physicians on June 2, 1942.

We gratefully acknowledge receipt of the following gifts donated to the College Library of Publications by Members:

Walter H. Baer, F.A.C.P., Captain, (MC), U. S. Army—1 reprint;
Dr. Jason Engels Farber (Associate), Buffalo, N. Y.—4 reprints;
Dr. T. Lyle Hazlett, F.A.C.P., Pittsburgh, Pa.—3 reprints;
Dr. Archibald L. Hoyne, F.A.C.P., Chicago, Ill.—14 reprints;
Dr. Vincent W. Koch, F.A.C.P., Janesville, Wis.—1 reprint;
Dr. Paul J. Lewis, F.A.C.P., Yakima, Wash.—1 reprint;
Dr. Walter B. Martin, F.A.C.P., Norfolk, Va.—4 reprints;
Dr. Oscar O. Miller, F.A.C.P., Louisville, Ky.—1 reprint;
Dr. Louis Bonner Owens, F.A.C.P., Cincinnati, Ohio—1 reprint;
Dr. Robert C. Page, F.A.C.P., Mount Vernon, N. Y.—3 reprints;
Dr. C. Graham Reid (Associate), Charlotte, N. C.—8 reprints;

Dr. Abraham Rudy, F.A.C.P., Boston, Mass.—17 reprints;
Dr. Leon Schiff, F.A.C.P., Cincinnati, Ohio—1 reprint;
Dr. Samuel Weiss, F.A.C.P., New York, N. Y.—3 reprints.

Dr. Charles F. Tenney Elected Regent

Dr. Charles F. Tenney, F.A.C.P., New York City, has been elected a member of the Board of Regents of the College to fill the vacancy caused by the elevation of Dr. Ernest E. Irons to the office of President-Elect. Dr. Tenney will serve until the next regular election.

Dr. Tenney has served several years as the College Governor for Eastern New York, a district in which the duties of the Governor are probably heavier than anywhere in the nation. His successor as Governor for Eastern New York will be named in the near future.

Regional Meeting of Nebraska Members

An informal Regional Meeting of Nebraska members of the College was held June 3, 1942, at the Omaha Club, Omaha, Nebr., under the Chairmanship of Dr. Warren Thompson, Governor for Nebraska. While the meeting was partially of a social character, it was utilized as a discussion meeting of problems affecting the College, with special reports from members who have taken A. C. P. postgraduate courses during the past year and those who were in attendance at the Annual Session of the College in St. Paul.

Although a large part of the attendance at this meeting came from the local membership, all outstate members were invited, and a fairly good number attended. Every member who was present at the St. Paul Session took part in the local informal program of discussion on clinics, panels, interesting papers and on postgraduate courses.

Regional Meeting of the College Members in Mississippi

During the meeting of the Mississippi State Medical Association Fellows and Associates of the American College of Physicians in Mississippi held their first regional meeting at a luncheon at the Robert E. Lee Hotel, Jackson, May 13, 1942, under the Governorship of Dr. John G. Archer, F.A.C.P., Greenville.

The guest speakers at this meeting were Dr. Fredrick A. Willius, F.A.C.P., Rochester, Minn., and Dr. Ralph Bowen, F.A.C.P., Houston, Tex. Dr. Willius spoke on "The Frequent Abuses of the Electrocardiograph" and Dr. Bowen spoke on "Allergy." Dr. Douglas D. Baugh, F.A.C.P., Columbus, Miss., was in charge of the program and led a round table discussion.

Of the nineteen College members in the State of Mississippi, twelve were present at this luncheon meeting. It was decided that the Mississippi members of the College would hold a regional meeting each year during the meeting of their state medical association.

American Gastro-Enterological Association Holds Forty-Fifth Annual Meeting

Under the Presidency of Dr. Russell S. Boles, F.A.C.P., Philadelphia, the American Gastro-Enterological Association held its forty-fifth annual meeting at Atlantic City, June 8–9, 1942. One of the highlights of the session was the presentation of the Friedenwald Medal to Dr. Max Einhorn, F.A.C.P., of New York City, the presentation being made by Dr. William Gerry Morgan, M.A.C.P., of Washington.

This Association has a total of 188 members, of all classes, of which 112 are Fellows and 8 are Associates of the American College of Physicians. Of its Officers during the past year, all but one are Fellows of the College, including Dr. Sara M. Jordan, Boston, 1st Vice President; Dr. A. H. Aaron, Buffalo, 2nd Vice President; Dr. John G. Mateer, Detroit, Treasurer; Dr. Julian M. Ruffin, Durham, Recorder; Dr. J. A. Bargen, Rochester, Minn., Secretary; Dr. Ernest H. Gaither, Baltimore, and Dr. A. C. Ivy, Chicago, Members of the Council; Dr. Walter L. Palmer, Chicago, Dr. Henry L. Bockus, Philadelphia, and Dr. John M. Blackford, Seattle, Committee on Admissions. Thirty-one places on the Atlantic City program were filled by Fellows or Associates of the College.

Under the Presidency of Dr. W. Paul Holbrook, F.A.C.P., Tucson, the Arizona State Medical Association held its annual meeting in Prescott, May 25–30, 1942. Among the guest speakers were:

Dr. Walter Bauer, F.A.C.P., Boston, Mass.—"Arthritis";
Dr. Noble Wiley Jones, F.A.C.P., Portland, Ore.—"Arteriosclerosis."

Dr. Jay M. Garner (Associate), Winnetka, Ill., spoke on "Interesting Proctoscopic Observations in Color" at a meeting of the Institute of Medicine of Chicago, May 22, 1942. Dr. Andrew C. Ivy, F.A.C.P., Chicago, Ill., presided.

Dr. Lee R. Woodward, F.A.C.P., Mason City, has been chosen President-Elect of the Iowa State Medical Society.

Dr. Thomas Addis, F.A.C.P., San Francisco, Calif., recently gave a Mayo Foundation Lecture in Rochester, Minn., on "The Treatment of Glomerulonephritis."

Dr. William Halsey Barker (Associate), Baltimore, Md., spoke on "The Sulfonamides" at a recent meeting of the South Carolina Medical Association at Columbia.

Among the speakers at the annual session of the American Academy of Tuberculosis Physicians held in Atlantic City, N. J., June 8–9, 1942, were:

Dr. Leo L. Hardt, F.A.C.P., Chicago, Ill.—"Gastroscopic Findings in Far Advanced Pulmonary Tuberculosis";
Carl W. Tempel (Associate), Major (MC), U. S. Army—"Pneumoperitoneum: Its Place in Collapse Therapy."

Dr. Lowell S. Selling, F.A.C.P., Detroit, Mich., spoke on "Psychopathology and Nutrition" at the 32nd Annual Meeting of the American Psychopathological Association in Boston, Mass., May 17–18, 1942.

The American Rheumatism Association held its 9th Annual Meeting in Atlantic City, N. J., June 8, 1942. Among those who participated in the program were:

Dr. Charles L. Short, F.A.C.P., and Dr. Walter Bauer, F.A.C.P., Boston, Mass.—"The Spinal Fluid Protein in Rheumatoid Arthritis";
Dr. R. Garfield Snyder, F.A.C.P., Dr. Willard Haywood Squires, F.A.C.P., and Dr. Cornelius Horace Traeger, F.A.C.P., New York, N. Y.—"The Treatment of Arthritis with an Agent Containing Massive Doses of Vitamin D";

Dr. Edward F. Rosenberg, F.A.C.P., and Dr. Philip S. Hench, F.A.C.P., Rochester, Minn.—"An Analysis of the Manner of Death Among Thirty Patients with Rheumatoid Arthritis";

Dr. Charles L. Steinberg (Associate), Rochester, N. Y.—"The Tocopherols (Vitamin E) in the Treatment of Primary Fibrositis."

The 8th Annual Meeting of the American College of Chest Physicians was held in Atlantic City, N. J., June 6–8, 1942, under the Presidency of Dr. Benjamin Goldberg, F.A.C.P., Chicago, Ill. Among the speakers were:

Dr. Robert W. Keeton, F.A.C.P., Chicago, Ill.—"Adequacy of Diabetic Management in the Presence of Infection";

Charles C. Hillman, F.A.C.P., Brigadier General, (MC), U. S. Army—"Tuberculosis in the Army";

Robert E. Duncan, F.A.C.P., Commander, (MC), U. S. Navy—"Tuberculosis in the Navy."

On June 8, the American College of Chest Physicians held a joint session with the American Broncho-Esophagological Association. Among the speakers at this meeting were:

Dr. Louis H. Clerf, F.A.C.P., Philadelphia, Pa.—"Adenoma (Mixed Tumor of the Bronchus)";

Dr. Ralph C. Matson, F.A.C.P., Portland, Ore.—"Bronchoscopic Aids in Chest Surgery";

Dr. J. Winthrop Peabody, F.A.C.P., Washington, D. C.—"Bronchoscopic Aids in Medical Conditions within the Chest."

Dr. Cornelius P. Rhoads, F.A.C.P., New York, N. Y., spoke on "The Chemical Aspects of Cancer" at the 43rd Annual Meeting of the American Proctologic Society in Atlantic City, N. J., June 7–9, 1942.

Under the Presidency of Dr. Milton B. Cohen, F.A.C.P., Cleveland, Ohio, the American Association for the Study of Allergy held its 20th Annual Meeting in Atlantic City, N. J., June 8–9, 1942. Among the speakers were:

Dr. Milton B. Cohen, F.A.C.P., Cleveland, Ohio—"The Basic Relationship of Allergy and Immunity";

Dr. Marion T. Davidson, F.A.C.P., Birmingham, Ala.—"The Source of the Activity of House Dust";

Dr. J. Warrick Thomas, F.A.C.P., Cleveland, Ohio—"Fatalities and Constitutional Reactions Following Use of Pontocaine";

Dr. George E. Harsh (Associate), San Diego, Calif.—"Studies of Tryptic and Peptic Digestion of Extracts of Giant Ragweed Pollen."

Dr. Cohen was one of the leaders at a round table discussion on "The Immunology of Allergy."

The 43rd Annual Meeting of the American Therapeutic Society was held in Atlantic City, N. J., June 5–6, 1942, under the Presidency of Dr. Harold S. Davidson, F.A.C.P., Atlantic City. Among those who participated in the program were:

Dr. Harold F. Robertson, F.A.C.P., Philadelphia, Pa.—"Bromide Intoxication";

Dr. Nathan S. Davis, III, F.A.C.P., Chicago, Ill.—"Ascorbic Acid in the Treatment of Essential Hypertension—Preliminary Report";

Dr. David Salkin, F.A.C.P., Hopemont, W. Va.—"The Natural History of Tuberculous Tracheobronchitis";

Dr. Harry E. Ungerleider, F.A.C.P., New York, N. Y., and Dr. Richard S. Gubner (Associate), Brooklyn, N. Y.—"Extrasystoles and the Mechanism of Palpitation."

Dr. Reginald Fitz, F.A.C.P., Boston Mass., was the principal speaker at the Society's banquet. Dr. Fitz spoke on "Something Curious in the Medical Line."

The American Heart Association held its 18th Scientific Session in Atlantic City, N. J., June 5–6, 1942. Dr. Paul D. White, F.A.C.P., Boston, Mass., President of the Association, was the principal speaker at the annual dinner. Dr. White spoke on "Pioneer Days of the Discovery of Heart Disease," and Harry G. Armstrong, F.A.C.P., Major, (MC), U. S. Army, delivered the George Brown Memorial Lecture on "The Effect of Flight on the Cardiovascular System."

Among those who presented papers at the scientific session were:

Dr. A. Wilbur Duryee, F.A.C.P., New York, N. Y.—"The Present Concept of Scleroderma and Its Allied Diseases";

Dr. William Goldring, F.A.C.P., New York, N. Y.—"The Reduction of Blood Pressure Associated with the Pyrogenic Reaction in Hypertensive Subjects";

Dr. Harold J. Stewart, F.A.C.P., New York, N. Y.—"The Effect of Cigarette Smoking on the Peripheral Blood Flow."

Dr. John E. Leach (Associate), Paterson, N. J., spoke on "The Effect of X-Ray Therapy on the Heart: A Clinical Study" at the 27th Annual Meeting of the American Radium Society in Atlantic City, N. J., June 8–9, 1942.

Among the Fellows of the College who spoke at the 26th Annual Meeting of the Association for the Study of Internal Secretions at Atlantic City, N. J., June 8–9, 1942, were:

Dr. Byron D. Bowen, Buffalo, N. Y.—"Metabolic Changes in Coexisting Diabetes Mellitus and Addison's Disease";

Dr. Charles H. Lawrence, Boston, Mass.—"The Treatment of Acne with Orally Administered Estrogens";

Dr. Willard O. Thompson, Chicago, Ill.—"Endocrine Regulation of Growth."

Dr. Louis E. Martin (Associate), Los Angeles, Calif., was chosen Vice President of the California Heart Association at its annual meeting in Del Monte, May 3, 1942.

Dr. George W. Thorn, F.A.C.P., has been appointed the Hersey Professor of the Theory and Practice of Physic, Harvard Medical School, and Physician-in-Chief of the Peter Bent Bringham Hospital, Boston, Mass., to succeed the late Dr. Soma Weiss, F.A.C.P. Prior to this appointment, Dr. Thorn was Associate Professor of Medicine at Johns Hopkins University School of Medicine, Baltimore, Md.

Dr. Alvan L. Barach, F.A.C.P., New York, N. Y., has been promoted to Associate Professor of Clinical Medicine, Columbia University College of Physicians and Surgeons.

Dr. Wann Langston, F.A.C.P., Oklahoma City, Okla., spoke on "Circulatory Emergencies," and Dr. James William Finch, F.A.C.P., Hobart, Okla., spoke on "Nausea and Vomiting Following Administration of Stilbestrol" at a recent joint meeting of the Custer County Medical Society and the Southwestern Oklahoma Medical Association.

Dr. Robert A. Cooke, F.A.C.P., New York, N. Y., spoke on "The Practitioner and the Allergy Problem" at the 131st Annual Meeting of the Rhode Island Medical Society at Providence, June 3–4, 1942. Dr. Charles F. Gormly, F.A.C.P., Providence, was named President of the Society.

Dr. John B. Youmans, F.A.C.P., Associate Professor of Medicine, Vanderbilt University School of Medicine, Nashville, Tenn., delivered the annual Stuart McGuire Lectures at the Medical College of Virginia, Richmond, May 7–8, 1942. Dr. Youmans spoke on "The Meaning of Nutrition" and "The Significance of Protein in the Diet."

During the session, which was conducted in coöperation with the Department of Clinical Education of the Medical Society of Virginia, the following also presented lectures:

Dr. Henry B. Mulholland, F.A.C.P., Charlottesville, Va.—"Nutrition Problems in Postoperative Patients";

Dr. Julian M. Ruffin, F.A.C.P., Durham, N. C.—"The Recognition of Mild or Early Vitamin Deficiencies";

Dr. Maxwell R. Berry, Jr. (Associate), Richmond, Va.—"The Significance and Treatment of Iron Deficiency Anemia."

The Canadian Medical Association held its 73rd Annual Meeting in Jasper Park, Alta., June 15–19, 1942. Among the speakers were:

Dr. Paul A. O'Leary, F.A.C.P., Rochester, Minn.—"The Treatment of Psoriasis" and "Dermatoscleroses";

Dr. Carleton B. Peirce, F.A.C.P., Montreal, Que.—"Recent Improvements in the X-Ray Diagnosis of Nontuberculous Pulmonary Diseases by Means of Bronchography";

Dr. W. Ford Connell, F.A.C.P., Kingston, Ont.—"Digitalis, Its Uses and Misuses."

The University of Pennsylvania School of Medicine, Philadelphia, held its annual Undergraduate Medical Association Day, April 9, 1942. Dr. O. H. Perry Pepper, F.A.C.P., Philadelphia, Pa., spoke on "The Medical Student and the War," and Dr. Carl J. Wiggers, F.A.C.P., Cleveland, Ohio, spoke on "War Gases."

Under the direction of Dr. Zacharias Bercovitz, F.A.C.P., New York, N. Y., the New York Post-Graduate Medical School conducted a course on Tropical Medicine, May 25–29, 1942. Among the lecturers were:

Dr. Thomas T. Mackie, F.A.C.P.—"Amebiasis: Diagnosis, Differential Diagnosis, Treatment and Prophylaxis";

Dr. Ward J. MacNeal, F.A.C.P.—"Yellow Fever: Diagnosis and Preventive Vaccination";

Dr. Zacharias Bercovitz, F.A.C.P.—"Tropical Hygiene."

Dr. Franklin G. Ebaugh, F.A.C.P., and Dr. Clarke H. Barnacle (Associate), both of Denver, Colo., spoke on "Fatalities Following Electric Convulsive Therapy" at the 68th Annual Meeting of the American Neurological Association held in Chicago, Ill., June 4–6, 1942.

Among the speakers at the 21st Annual Meeting of the American Society of Clinical Pathologists, Philadelphia, Pa., June 4–7, 1942, were:

Dr. Israel Davidsohn, F.A.C.P., Chicago, Ill.—"The Rh Factor: An Antigenic Analysis";

Dr. Samuel A. Levinson, F.A.C.P., Chicago, Ill.—"Cerebral Injuries by Mechanical Violence."

Dr. Edward A. Strecker, F.A.C.P., Philadelphia, Pa., Professor and Head of the Department of Psychiatry at the University of Pennsylvania School of Medicine and President-Elect of the American Psychiatric Association, delivered the principal address at the formal dedication of the Illinois Neuropsychiatric Institute in Chicago, June 6, 1942. Dr. Strecker spoke on "Neuropsychiatric Perspectives."

Dr. Andrew C. Ivy, F.A.C.P., Chicago, Ill., spoke on "The Physiology of the Gall-bladder" and "The Physiology of the Thyroid Gland" at the recent Annual Spring Clinical Conference of the Pottawatomie County Medical Society, at Shawnee, Okla.

Dr. William H. Sebrell, Jr., F.A.C.P., Washington, D. C., was elected Treasurer of the American Institute of Nutrition at its meeting in Boston, Mass., April 1, 1942.

Dr. Herbert T. Kelly, F.A.C.P., Philadelphia, Pa., presented a paper on "Nutrition as It Applies to General Disease," illustrated by a motion picture in natural color, at a meeting of the Gloucester County Medical Society, Woodbury, N. J., May 21, 1942.

The Omaha Mid-West Clinical Society will hold its 1942 meeting in Omaha, Nebr., October 26–30. The meeting will consist of local lecture periods, round table discussions, scientific and technical exhibits, and a symposium on "The Newer Concepts Regarding Hypertension and Its Treatment."

Dr. Joseph T. Beardwood, Jr., F.A.C.P., Philadelphia, Pa., was named President of the American Diabetes Association at its recent meeting in Atlantic City, N. J.

Dr. Sara M. Jordan, F.A.C.P., Boston, Mass., was elected President of the American Gastro-Enterological Association at its recent meeting in Atlantic City, N. J. Dr. Jordan is the first woman ever to be so honored.

Mr. H. J. Cowell of Lea & Febiger, Philadelphia, Pa., has been elected President of the Medical Exhibitors Association. Mr. Cowell succeeds Mr. C. H. Wantz of the General Electric X-Ray Corporation, Chicago, Ill., who had served for three terms.

James O. Gillespie, F.A.C.P., Colonel, (MC), U. S. Army, stationed at the Sternberg General Hospital, Manila, P. I., has been reported missing in action.

Dr. Joseph H. Barach, F.A.C.P., Pittsburgh, Pa., addressed the Clearfield County Medical Society at Clearfield, Pa., on May 21, 1942. His subject was "A Clinical Consideration of Functional and Organic Diseases of the Blood Vessels."

Dates of A. C. P. Annual Session Announced

The American College of Physicians will hold its Twenty-seventh Annual Session in Philadelphia, Pa., April 13–16, inclusive, 1943. Dr. George Morris Piersol of Philadelphia has been appointed General Chairman.

A change will be instituted in regard to the length of the Session. Heretofore the Session has opened Monday afternoon and continued through Friday afternoon. Due to the War and consequent added burdens on physicians' time, as well as expenses, the 1942 Session will be condensed into four days, Tuesday through Friday. The meeting will be arranged so that there will be no appreciable loss in the content of the program; members will save one day in time and expense, and by installing the exhibits on Monday, instead of over the weekend as heretofore, exhibitors will be spared double overtime labor charges.

OBITUARIES

DR. FREDERIC M. JOHNSON

Dr. Frederic M. Johnson was born in New York, N. Y., August 5, 1874. He received his M.D. degree from the Syracuse University College of Medicine in 1904, and served his internship at St. Joseph's Hospital, Providence, R. I., 1904–1905. From 1907–1911 he was Clinical Assistant in Diseases of the Digestive System, during 1911, Instructor, and from 1912–1917, Lecturer and Adjunct Professor of Diseases of the Digestive System, at New York Polyclinic Medical School and Hospital. From 1906 until his death on April 12, 1942, he was a Member of the Staff of St. John's Riverside Hospital, Yonkers, serving in various capacities, and since 1927 he was Director of Gastro-enterology at this institution. He was also Gastro-enterologist at the Yonkers Professional Hospital, Consulting Gastro-enterologist at the Gray Oaks and Yonkers City Hospitals, and a Member of the Courtesy Staff of Yonkers General and St. Joseph's Hospitals. Dr. Johnson spent the summers of 1926, 1931, 1933 and 1934 doing postgraduate work in hospitals in London and Paris.

Dr. Johnson was a member of the Westchester County Medical Society, the New York State Medical Society, the Yonkers Academy of Medicine, of which he was President from 1935–1936, the New York Academy of Medicine, the New York Gastro-enterological Association, the National Society for Advancement of Gastro-enterology, a Fellow of the American Medical Association, Diplomate of the American Board of Internal Medicine. He became an Associate of the American College of Physicians in 1925 by virtue of his membership in the American Congress on Internal Medicine.

Dr. Johnson was a member of Masonic Lodge, Past Master of Nepperhan Lodge, member Terrace City Chapter, Yonkers Commandery and Mecca

Temple of New York. He was a Director of the Yonkers Savings and Loan Association and a Vestryman at St. Andrew's Memorial Church.

Dr. Johnson is survived by his widow and two daughters.

CHARLES F. TENNEY, M.D., F.A.C.P.,
Governor for Eastern New York

DR. ARCHIBALD ADDISON ALEXANDER

Dr. Archibald Addison Alexander, F.A.C.P., of Oakland, Calif., died at his home on January 17, 1942. Dr. Alexander was a native Californian, as he was born at San Ramon, Calif., May 28, 1880. After graduating from high school in his native community, he attended the University of California, receiving his A.B. degree in 1902, and his M.D. degree from the University of California Medical School in 1907. He was an Instructor in Medicine at the Oakland College of Medicine from 1908–11. He became an Associate in Medicine at the Samuel Merritt Hospital, Oakland, in 1912, and served until 1931, when he became Chief Cardiologist to the Hospital. He was also Cardiologist to the Peralta Hospital of Oakland. He served as an Associate in Medicine at the Alameda County Hospital from 1928 until his death. He was also Consultant in Cardiology at the Children's Hospital of the East Bay.

Dr. Alexander was a Diplomate of the American Board of Internal Medicine, a member of the Alameda County Medical Society, the California State Medical Association, the California Academy of Medicine and the American Medical Association. He became a Fellow of the American College of Physicians in 1935.

Although interested in cardiology, Dr. Alexander was a keen student in the entire field of internal medicine and a firm believer in a broad base for specialization. He was a consistent, diligent worker, very faithful and loyal to the institutions he served, never seeking or asking praise or reward.

ERNEST H. FALCONER, M.D., F.A.C.P.,
Governor for Northern California

DR. JULIUS PETER DWORETZKY

Dr. Julius Peter Dworetzky of Liberty, New York, was born December 24, 1885, in Lido, Russia, and died April 20, 1942.

In 1910 Dr. Dworetzky received his M.D. degree from the Long Island College Hospital and served his internship in this hospital from 1910–12. From 1913–18, Dr. Dworetzky was Resident Physician at the Municipal Sanatorium, Otisville, N. Y., and later became Visiting Physician. He served as Consulting Physician, Ulster County Tuberculosis (Kingston), St. Francis (Port Jervis), Elizabeth A. Horton Memorial (Middletown), and St. Clare's (New York City) Hospitals; he was Visiting Physician,

Maimonides Hospital, Liberty, and was Medical Examiner for the Veterans Administration. A few years ago he became Director of Medicine at the Municipal Sanatorium.

During World War 1, Dr. Dworetzky served as a Captain with the American Red Cross and with the Rockefeller Commission for the Control of Tuberculosis in France.

Dr. Dworetzky was a member of the New York State Medical Society, the National Tuberculosis Association, the American Laryngological, Rhinological and Otological Society, the American College of Chest Physicians, a Fellow of the American Medical Association; a Diplomate of the American Board of Internal Medicine and the American Board of Otolaryngology; and a Fellow of the American College of Physicians since 1931.

Dr. Dworetzky made several original contributions to the literature in the field of laryngeal tuberculosis.

CHARLES F. TENNEY, M.D., F.A.C.P.,
Governor for Eastern New York

MINUTES OF THE BOARD OF REGENTS

ST. PAUL, MINN.

APRIL 19, 1942

The first meeting of the Board of Regents, in conjunction with the Twenty-sixth Annual Session of the American College of Physicians, convened in the Municipal Auditorium, St. Paul, Minn., Sunday afternoon, April 19, 1942, at 2:30 p.m., with President Roger I. Lee presiding and Mr. E. R. Loveland acting as Secretary, and with the following members in attendance:

Roger I. Lee	*President*
James E. Paullin	*President-Elect*
Thomas T. Holt	*Second Vice-President*
William D. Stroud	*Treasurer*
George Morris Piersol	*Secretary-General*
Francis G. Blake	
Reginald Fitz	
William J. Kerr	
Charles T. Stone	
J. Morrison Hutcheson	
T. Homer Coffen	
Ernest E. Irons	
Jonathan C. Meakins	
Charles H. Cocke	
John A. Lepak	*General Chairman*
E. R. Loveland	*Executive Secretary*

At this point President Lee introduced Dr. Lepak, the General Chairman of the St. Paul Session, whereupon Dr. Lepak made various announcements in regard to the clinics, hotels, transportation facilities and other matters affecting the meeting.

The Secretary read abstracted Minutes of the preceding meeting of the Board of Regents, December 14, 1941, which, by resolution, were approved as read.

President Lee called for communications.

Secretary Loveland then read communications from Drs. Samuel E. Munson, James D. Bruce, M. C. Pincoffs, D. S. Lewis and David Barr, members of the Board of Regents who were prevented from being present. Among other communications presented by the Secretary were the following:

(1) A letter from the Radiological Society of New Jersey, containing a resolution affirming that that Society has gone on record as being unalterably opposed to an all inclusive hospital service plan including medical, x-ray and laboratory services.

(2) A letter from the Office of the Surgeon General of the Army concerning contemplated training programs in certain fields of specialty and for the allotment of officers to various postgraduate courses and clinics.

(3) A letter from Dr. Virgil E. Simpson, F.A.C.P., Louisville, Ky., concerning activities of the College in connection with the U. S. Pharmacopoeia, standardization of hospitals, nomenclature of diseases and other services.

(4) A formal report from Dr. Charles F. Tenney, F.A.C.P., official College delegate and spokesman for the College delegation to the U. S. Pharmacopoeial Convention as follows:

"A meeting of the Medical-Pharmaceutical Convention took place at the Hotel Statler, Cleveland, Ohio, on April 6, 1942, under the auspices of the Joint Committee of the American Medical Association and the American Pharmaceutical Association. Drs. Charles F. Tenney, Edward G. Spalding and Torald H. Sollmann were the delegates from the American College of Physicians.

"The afternoon of April 6 was given over to the reading of papers and a most excellent paper was given by Dr. Howard Dietrick, of Cleveland, on the 'Evolution of the Apothecary.' From an historical standpoint it was excellently presented, starting from the earliest periods, B.C., and carrying them on up to the present time. Dr. E. F. Kelly, Chairman of the Board of Trustees of the United States Pharmacopoeial Association and Secretary of the American Pharmaceutical Association, traced out very clearly the 'Trends of Pharmaceutical Practice,' stating the total number of Pharmaceutical Schools and the number of men graduated from these schools each year. He also stated that he hoped very soon they would have practical courses following their graduation, similar to internships in hospitals which would extend for a period of about two years. The third paper, 'Is the Program of Pharmaceutical Education Justified?,' was given by Dr. Robert C. Wilson, Dean of the School of Pharmacy of the University of Georgia, Athens, Georgia. This paper explained how justified was the interest taken in the progress for pharmaceutical education and that it had been warmly adopted by the different schools of pharmacy in the different universities throughout the United States. Dr. Torald H. Sollmann, F.A.C.P., Dean, Professor and Director of the Department of Pharmacology and Materia Medica, Western Reserve University School of Medicine, was the presiding officer for the afternoon meeting, and general discussions followed the reading of the papers. Among the speakers was Dr. Morris Fishbein, Editor of the American Medical Association, who seemed to carry the impression that the pharmacists would eventually have to rely upon hospitals and other institutions rather than preparing their prescriptions in drug stores. He thought the combining of a restaurant and a drug store was bad practice and for that reason pharmacy was being pushed backward rather than forward. The meeting was adjourned at 5:30 p.m.

"The evening session opened at 6:30 p.m. with a dinner which was largely attended by the members present, Dean B. V. Christensen, presiding.

"The address of the evening was given by Dr. Fishbein on 'Status of Medicine and Pharmacy in the War—and After.' He talked rapidly and fluently for about forty-five minutes, using about one hundred and fifty words per minute. He stated that this was the first joint meeting in history of representatives of the American Medical Association and the American Pharmaceutical Association. He gave a most excellent discussion not only with regard to his title, but also recommended that the Medical Procurement and Assignment Service, which is making an inventory of all persons practicing medical, dental, or veterinary professions, should extend its services to include 'the correlated pharmaceutical profession, physical therapists, laboratory specialists, and roentgenological technicians. By suitable collaboration of this agency with the National Roster of Scientific and Trained Personnel,' said Dr. Fishbein, 'we will be able to meet more adequately the needs of our fighting forces.'

"Dr. Fishbein told of the recent appointment of an advisory committee on drugs and supplies of the division of medical sciences of the National Research Council. It was thought not long ago, he said, that this nation had a three year supply of such drugs as quinine and morphine, but that estimate did not take into account the entrance of troops into areas where contact was made with such diseases as leishmaniasis, kala azar, African sleeping sickness and yellow fever.

"The evening meeting adjourned about 9:30 p.m. The above papers will no doubt be published in the near future, and any of the Fellows who are interested may obtain copies if they write to Dr. Cary Eggleston, President of the United States Pharmacopoeial Convention, 125 East 74th Street, New York City.

"The Adjourned Session of the 1940 Decennial Meeting of the United States Pharmacopoeial Convention, reconvened at the Hotel Statler, Cleveland, Ohio, on April 7, 1942, with Dr. Cary Eggleston, President, in the Chair.

"After the meeting was called to order, Dr. Morris Fishbein requested to be recognized. He moved that inasmuch as no changes could be made in the Proposed Constitution until 1950 that no discussion of the Constitution take place at this time. It was seconded and carried.

"However, the By-Laws and their changes could be acted upon at this meeting, so each chapter and article of the By-Laws was read, voted upon, changes made, and finally adopted as the By-Laws governing the Pharmacopoeial Convention. It was then voted to read the new Constitution. This was done but no comments or discussions were permitted. The changes that have been made in the By-Laws were circulated in typewritten form and copies will be available for distribution to the members probably within a short time. All this work had been compiled and brought up to date under the guidance of legal advisers.

"The Committee on Revision of the U. S. Pharmacopoeia stated that the U.S.P. No. XII could be ready for distribution by July 1, 1942. Circulars were distributed in typewritten form of articles advised for the U.S.P. No. XII with Latin and English titles. There was some discussion as to the shortage of drugs because of inability to get them and also the large amount which are taken and sent to our forces over-seas. The meeting adjourned at 12:40 p.m."

Respectfully submitted,

(Signed) CHARLES F. TENNEY

Delegates: CHARLES F. TENNEY, *Chairman*
EDWARD G. SPALDING
TORALD H. SOLLMANN"

SECRETARY LOVELAND: During the past year a movement was started to greatly reduce the number of medical agencies represented in the U. S. Pharmacopoeial Convention; in fact, to eliminate practically all societies, including the American College of Surgeons and the American College of Physicians, but to retain the American Medical Association and its constituent state medical societies. It was not entirely clear whether or not this movement was directed against some of the special societies which held membership, but there have been many who felt that this College should retain its representation, because there is no group of physicians that has a more definite interest and part both in prescribing and teaching in this important field. Dr. Tenney, as spokesman, represented the College and its interests and his report reveals there will be no change in the next eight years. I would suggest, however, that this report be incorporated in the minutes and published.

PRESIDENT LEE: If there are no objections it will be so ordered.

The next item of business will be the appointment of a member of the American Board of Internal Medicine for the term 1942–45. The President was advised that the term of Dr. David P. Barr would expire June 30, 1942. . . . It is found that Dr. Barr has served only one full term and can be reëlected to the Board.

DR. WILLIAM D. STROUD: I move that Dr. Barr's name be recommended for reappointment to the American Board of Internal Medicine for the next three years.

DR. GEORGE MORRIS PIERSOL: I second Dr. Stroud's motion recommending the reappointment of Dr. Barr.

PRESIDENT LEE: . . . All those in favor of recommending to the American Board of Internal Medicine the name of Dr. David P. Barr, of New York, as the repre-

sentative of this College on the American Board of Internal Medicine for the term 1942–45 will say "aye"; opposed "no."

The motion was carried.

PRESIDENT LEE: The next item of business is the report of the Secretary-General.

DR. GEORGE MORRIS PIERSOL, *Secretary-General:* Since the last meeting of the Board 16 Fellows and 2 Associates have been lost by death, namely:

Fellows:

Austin, Albert Elmer, Old Greenwich, Conn., January 26, 1942
Cutter, William Dick, Chicago, Ill., January 22, 1942
Helm, Jesse Bundren, M.C., U. S. Navy, November 26, 1941
Jones, Louise Taylor, McLean, Va., December 21, 1941
Lambert, Samuel Waldron, Sr., New York, N. Y., February 9, 1942
Leech, Frank, Washington, D. C., February 4, 1942
Marbury, Charles Clagett, Washington, D. C., December 10, 1941
Niles, Walter Lindsay, New York, N. Y., December 22, 1941
* Peters, LeRoy Samuel, Albuquerque, N. M., December 17, 1941
Reque, Peter Augustin, Brooklyn, N. Y., December 4, 1941
Ryan, William Joseph, Pomona, N. Y., February 20, 1942
Sleyster, Rock, Wauwatosa, Wis., March 7, 1942
Stoddard, Charles Hatch, Milwaukee, Wis., December 17, 1941
Sylvester, Charles Bradford, Portland, Maine, December 18, 1941
Tracy, Martha, Philadelphia, Pa., March 22, 1942
Weiss, Soma, Boston, Mass., January 31, 1942

Associates:

Fisler, Harry Cattell, Easton, Pa., February 20, 1942
Wolf, Isadore Julius, Kansas City, Mo., December 17, 1941

This brings the total since the last Annual Session to 48 Fellows; 5 Associates; total, 53. Comment: for the preceding year, 47 Fellows; 7 Associates, or a total of 54 died.

The following twelve additional Life Members are also reported since the last meeting of this Board:

Siegfried Block, Brooklyn, N. Y.
William Hall Bunn, Youngstown, Ohio
F. Gorham Brigham, Brookline, Mass.
Samuel Lee Gabby, Elgin, Ill.
George Curtis Crump, Asheville, N. C.
Henry L. Ulrich, Minneapolis, Minn.
Edward William Hayes, Monrovia, Calif.
Frederick Edward Hudson, Stamford, Tex.
H. Leon Jameson, Philadelphia, Pa.
James D. Bruce, Ann Arbor, Mich.
Ardrey W. Downs, Edmonton, Alta., Canada
Maurice Lewison, Chicago, Ill.

At the preceding meeting of this Board, the Secretary-General reported 4 new Life Members, which makes a total since the last Annual Session of 16; a grand total of 183, of whom 17 are deceased, leaving a balance of 166.

PRESIDENT LEE: This is a report to the Board of Regents and requires no action. I now call for the report of the Committee on Credentials. The list of recommendations to be presented is already in your hands.

* Governor for New Mexico.

DR. GEORGE MORRIS PIERSOL, *Chairman:* The Committee on Credentials has met twice since the preceding Regents' meeting, once in Philadelphia on March 22, 1942, and again at St. Paul on April 19, 1942. In your hands is a typewritten list of candidates who are recommended for election to Fellowship and Associateship. The following is an analysis of the candidates considered on March 22:

A. Candidates for FELLOWSHIP:

Recommended for election:		
Advancement from Associateship	103	
Direct election to Fellowship	14	117
Elect Associate First		1
Deferred for Further Investigation, Maturity, etc.		15
Rejected		1
		134

B. Candidates for ASSOCIATESHIP:

Recommended for Election	76
Deferred for Further Credentials	9
Rejected or Withdrawn	9
	94

An analysis of the candidates considered on April 19 is as follows:

A. Candidates for FELLOWSHIP:

Recommended for election:		
Advancement from Associateship	46	
Direct election to Fellowship	2	48
Deferred for Further Investigation, Maturity, etc.		10
Rejected		1
		59

B. Candidates for ASSOCIATESHIP:

Recommended for Election	44
Deferred for Further Credentials	0
Rejected or Withdrawn	5
	49

Chairman Piersol presented each group individually, discussing special cases, and on his motion, seconded and carried, the entire list was elected with a covering resolution as follows:

RESOLVED, that the following list of 165 candidates be and herewith are elected to Fellowship in the American College of Physicians: (ED. NOTE: This list was published in the May, 1942, issue of this journal.)

RESOLVED, that the following list of 120 candidates be and herewith are elected to Associateship in the American College of Physicians: (ED. NOTE: This list was published in the May, 1942, issue of this journal.)

DR. PIERSOL, *Chairman:* Several other matters came before the Committee for consideration. The first is a report on candidates elected to Associateship on April 18,

1937, whose period of probation has now expired. Seven Associates elected at that time have not presented their credentials, or their credentials have not been accepted, and, therefore, are herewith recorded as dropped under provisions of the By-Laws.

A final analysis of the disposal of the Associates elected April 18, 1937, is as follows:

Advanced to Fellowship	112
Dropped for Failure to Qualify or to Present Credentials	7
Resigned	0
Deceased	0
	119

Every reasonable effort has been made to influence Associates to qualify for Fellowship, and if they have failed to do so it has been due to their own indifference or carelessness.

A formal resolution offered by Dr. Piersol, seconded by Dr. Cocke, and carried, confirmed the dropping of the seven Associates in accordance with the provisions of the By-Laws.

DR. PIERSOL, *Chairman:* The Committee recommends to the Board of Regents that Dr. Richard H. Dalrymple be reinstated to Fellowship.

. . . On motion by Dr. Stroud, seconded by Dr. Kerr and regularly carried it was resolved that Dr. Richard H. Dalrymple, Fond du Lac, Wisconsin, be herewith reinstated to Fellowship in the American College of Physicians. . . .

President Lee announced that since Dr. Paullin and Dr. Morgan, Chairmen of the Committee on Public Relations and Advisory Council on Medical Education, respectively, had not yet arrived, their reports would be delayed until the next meeting. He called upon Dr. Blake as Chairman of the Committee on Fellowships and Awards for reports.

DR. FRANCIS G. BLAKE: I submit a report of the Committee on Fellowships and Awards. Of the three Fellowships awarded by the American College of Physicians at the meeting of the Board of Regents on December 14, 1941, two were accepted as follows:

1. Dr. James Hopper, Jr., to begin work September 1, 1942, in the Department of Internal Medicine, Yale University School of Medicine, under the direction of Dr. John P. Peters, on "A Comparison of the Carbon Monoxide and Dye Methods of Blood Volume Determination."
2. Dr. Joseph L. Lilienthal, Jr., to begin work September 1, 1942, in the Department of Medicine, Vanderbilt School of Medicine, under the direction of Dr. E. M. Harvey on "A Study of Myasthenia Gravis and Related Problems in Neuromuscular Transmission in Man."

The third award to Dr. Charles P. Emerson, Jr., was declined because of military service. Following Dr. Emerson's declination of the fellowship, award was made to the alternate, Dr. Carl G. Heller, to begin work July 1, 1942, at Wayne University College of Medicine, under the direction of Dr. Gordon B. Myers on the physiology of hypo- and hypergonadism in relation to hypo- and hyperpituitarism in human males and females.

Dr. Allen D. Bass, one of the American College of Physicians' fellows for the current year, tendered his resignation effective January 1, 1942, to engage in a war research project, and his resignation was accepted.

Respectfully submitted,

FRANCIS G. BLAKE, M.D., *Chairman,*
Committee on Fellowships and Awards

On motion by Dr. Blake, seconded by Dr. Meakins and regularly carried this report was adopted.

PRESIDENT LEE: Do you have a further report to make, Dr. Blake?

DR. BLAKE: I attended the meeting of the Advisory Council on Medical Education in Chicago on February 15. It was a relatively brief meeting, the discussion being largely concerned with the acceleration of the medical school course, the adjustment of internships to the accelerated program, and problems arising from conflict with various state laws relative to the required length of medical education.

Only two actions were taken: one, a vote expressing appreciation of the cooperation of Selective Service and the Surgeons General, in their collaboration with the Committee on Preparedness of the Association of American Medical Colleges in working out a satisfactory adjustment which will permit medical students to complete their education; two, an endorsement of certain actions of the Association of American Medical Colleges relative to the accelerated program of medical education, as follows: that there should be no lowering of requirements for admission to the medical schools because of the accelerated program; that the Executive Council of the Association shall negotiate with the Federal Bureau of Education with respect to the possibility of obtaining loans for medical students who may need additional financial assistance because of inability to work during the summer months; that the length of internships be not reduced below twelve months.

PRESIDENT LEE: This report requires no action. It will be placed on file.

Dr. Fitz, will you report for the Committee on the ANNALS OF INTERNAL MEDICINE?

DR. REGINALD FITZ: Mr. President, the Editor, Dr. M. C. Pincoffs, has been called to active service. It has been the feeling of the Committe on the ANNALS that it would be proper for the Committee to recommend to the Board of Regents that the Editor be given leave of absence during whatever time he may be away in order that his service as Editor may be obtained when he returns. We make that recommendation.

The second point that comes up concerns what may be done during his absence. The Editor communicated with the Chairman, and the Chairman with the President. I am informed that tentatively the editorial work of the ANNALS has been left in the hands of Dr. Paul Clough, Assistant Editor, until this matter is officially settled.

Dr. Clough is perfectly competent and well trained to take care of the editorial work. While Dr. Pincoffs is away an Assistant Editor should be appointed to work under Dr. Clough, and in that way the continuous policy of the ANNALS can be maintained.

Dr. Pincoffs has already submitted the name of an Assistant Editor to the Committee on the ANNALS for consideration, but such nomination has not been submitted to me. Dr. Pincoffs reports that the affairs of the ANNALS appear to be in good order. The Editor's office has on hand a large amount of very good material, so that if the output of scientific work falls off in the near future there will still be a good deal of material in the Editor's hands, as a backlog, for several months to come.

And, finally, Dr. Pincoffs wishes very much to extend to the Committee and to the Regents his appreciation of their support through the years he has been Editor. He feels that to leave the ANNALS in the hands of Dr. Paul Clough is the best available solution, and he hopes that the periodical will continue while he is away.

I should like to make a motion that Dr. Pincoffs be given a leave of absence.

DR. MEAKINS: I second the motion.

DR. STROUD: May I ask, Mr. President, if there is to be any new arrangement made concerning the salary to be paid to the Editor, or whether that automatically, in the present amount, shall go to Dr. Clough?

DR. FITZ: In Dr. Pincoffs' letter to Dr. Palmer, Chairman of the Committee, the understanding was that Dr. Clough, if his appointment is confirmed by the Board of

Regents, will be in charge of the ANNALS during Dr. Pincoffs' absence and will receive the same salary as Dr. Pincoffs had been receiving, and that the Assistant Editor shall receive the same salary Dr. Clough previously received. Therefore, the budgetary arrangement will remain constant.

PRESIDENT LEE: We have been very fortunate, indeed, to have Dr. Clough available as Acting Editor. Are there any other questions? The first motion concerns an indefinite leave of absence to Dr. Pincoffs as Editor. All those in favor will say "aye"; opposed "no."

The motion was carried.

DR. FITZ: I move that Dr. Paul Clough be appointed by the Board of Regents as Acting Editor during Dr. Pincoffs' absence at the same salary which Dr. Pincoffs previously received.

The motion was seconded by Dr. Meakins and unanimously carried.

On motion by Dr. Cocke, seconded by Dr. Stroud and regularly carried it was resolved that Dr. Paul Clough as Acting Editor shall be empowered to nominate an Assistant Editor to the Committee on the ANNALS OF INTERNAL MEDICINE for official approval.*

PRESIDENT LEE: The Executive Secretary will report on increased printing charges for the journal.

SECRETARY LOVELAND: Beginning July 1, 1942, the printers request permission to make an additional charge of $2.65 per form of 32 pages, per thousand copies, which will amount to approximately $90.00 per issue; and also permission to increase cost by approximately $4.50 per issue for cover stock. These two increments will amount to approximately $1,100.00 to $1,200.00 per annum. Since our original printing contract was authorized by the Regents, I believe this alteration should be first approved by the Regents and herein recorded.

On motion by Dr. Meakins, seconded by Dr. Cocke, it was resolved that the printing contract of the Lancaster Press be altered in the form and amount suggested by the Executive Secretary.

Dr. Ernest E. Irons, Chairman, American Board of Internal Medicine, distributed several charts showing results of examinations, relative ages and other matters of interest in the experience of that Board in conducting its work. He referred to the probability of some lean years in the near future, due primarily to the war.

DR. ERNEST E. IRONS: About a year ago the American Board of Internal Medicine discussed with the Board of Regents of the College a reduction in the examination fee, but at that time felt that in view of the added expense for examination in sub-specialties, it would be well to wait one year for results. Our experience now indicates that receipts from sub-specialties' examinations have been just about enough to cover the expenses. However, we are now prepared to consider the reduction of the examination fee from $40.00 to $30.00, and $10.00 for certification, making a total expense of $40.00 instead of $50.00, provided the College cares to consider this program.

Our fee for examination is far lower than that of most of the other special Boards, but the volume that we have to handle makes possible the consideration of reduction.

PRESIDENT LEE: You make no motion, Dr. Irons, you simply desire a discussion on this matter?

DR. IRONS: The Board of Regents brought this matter up a year ago, asking the American Board of Internal Medicine to make some reduction. If the Regents desire to make a reduction in the examination fee, the American Board of Internal Medicine is now in a position to go along.

* N. B.—Subsequently Dr. W. Halsey Barker, of Baltimore, was formally appointed Assistant Editor beginning May 1, 1942; Dr. Clough assumed the title of Acting Editor on May 1, 1942.

DR. WILLIAM J. KERR: Dr. Irons, there is a reserve of about $27,000 in your Treasury, and a gain of $4,000 during the past year in spite of the sub-specialty Board examinations. It seems to me that the College and the Board could combine in making some reduction in fees for the candidate, and this would be a wise move. Whether or not other specialty Boards do this, I think ours should take the lead.

DR. GEORGE MORRIS PIERSOL: Mr. President, the Finance Committe should carefully consider this and bring in a report on its advisability.

DR. CHARLES H. COCKE: Mr. Chairman, it seems to me that in view of the situation that is going to involve a great many men now, we want to act very carefully. Dr. Piersol suggested that this should receive, accordingly, a careful examination. There is going to be considerable pressure for the reduction of College fees. This has already been brought to my attention as a Governor, and I recommend the proper study of this problem by the Finance Committee.

DR. IRONS: Mr. Chairman, we are all aware that the reduction Dr. Cocke points out involves also other things, and we are now talking about the amount the man pays for admission. Pressure on the College is going to be on the amount he pays after he is admitted.

SECRETARY LOVELAND: Is there any variation in the examination fee for different classes of physicians, such as those on active service or otherwise?

DR. IRONS: No.

PRESIDENT LEE: The Chairman of the Finance Committee, Dr. Pepper, is not present. At the last meeting the Finance Committee was prepared to be liberal in the treatment of those who are called to active service, but found itself in a quandary as to reducing annual dues of temporary officers below the annual dues of those who are officers of the armed forces permanently. Furthermore, there are going to be more people employed by the Government. That too has been carefully considered by the Finance Committee, and this preferential list for a low fee, lower than that established for the present regular officers of the Army and Navy, put the Finance Committee in a great deal of a quandary. The Board of Regents did vote that when a man enters on active service his fees shall be the same as for those in the regular medical corps of the Army and Navy.

I received a letter from Chairman Pepper who merely stated that as Chairman of that Committee he was prepared to be as liberal as possible to these temporary members of the armed forces, but that it seems difficult to find a satisfactory formula.

DR. WILLIAM D. STROUD: Mr. President, I move that since the Finance Committee is reporting at the Tuesday afternoon session of this Board, that Committee confer with Dr. Irons and bring in a recommendation for consideration by the Regents.

The motion was seconded by Dr. Paullin and unanimously carried.

There being no further business, President Lee read various announcements and the meeting adjourned at 4:20 p.m.

Attest: (*Signed*) E. R. LOVELAND,
Secretary